=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 16:09:17 ON 13 FEB 2004
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 6, 2004 (20040206/UP).

=> file caplus

FILE 'CAPLUS' ENTERED AT 16:09:23 ON 13 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Feb 2004 VOL 140 ISS 7
FILE LAST UPDATED: 11 Feb 2004 (20040211/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 16:09:26 ON 13 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 13 Feb 2004 VOL 140 ISS 7
FILE LAST UPDATED: 11 Feb 2004 (20040211/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 16:09:44 ON 13 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb  6, 2004 (20040206/UP).

=> d que l41
L1   (         3)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("RASAMOELISOLO M"/AU OR
                   "RASAMOELISOLO MICHELE"/AU)
L2   (        47)SEA FILE=HCAPLUS ABB=ON  PLU=ON  "BRIDON D"/AU OR ("BRIDON
                   DOMINIQUE"/AU OR "BRIDON DOMINIQUE P"/AU)
L3   (         9)SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("THIBAUDEAU K"/AU OR
                   "THIBAUDEAU KAREN"/AU)
L4   (      1057)SEA FILE=CAPLUS ABB=ON  PLU=ON  ("HUANG X"/AU OR "HUANG X
                   B"/AU OR "HUANG X C"/AU OR "HUANG X D"/AU OR "HUANG X F"/AU OR
                   "HUANG X G"/AU OR "HUANG X H"/AU OR "HUANG X J"/AU OR "HUANG X
                   K"/AU OR "HUANG X L"/AU OR "HUANG X M"/AU OR "HUANG X M H"/AU
                   OR "HUANG X M HENRY"/AU OR "HUANG X N"/AU OR "HUANG X P"/AU OR
                   "HUANG X PING"/AU OR "HUANG X Q"/AU OR "HUANG X R"/AU OR
                   "HUANG X S"/AU OR "HUANG X T"/AU OR "HUANG X TRENT"/AU OR
                   "HUANG X W"/AU OR "HUANG X X"/AU OR "HUANG X Y"/AU OR "HUANG X
                   Z"/AU) OR "HUANG XICAI"/AU
L12  (        47)SEA FILE=HCAPLUS ABB=ON  PLU=ON  "BRIDON D"/AU OR ("BRIDON
                   DOMINIQUE"/AU OR "BRIDON DOMINIQUE P"/AU)
L13  (        18)SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND ?PEPTIDE?/TI
L14           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND LASTING/TI
L37          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR L3
L38           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 AND ?BLOOD?
L39           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L2
L40           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L37
L41          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR L38 OR L39 OR L40

=> d ibib ab l41 1-16
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y
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appears in application title

Bridon ↵ Ras. +th. Huang + Bridon Huang + (Ras. or th.)

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L41  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:101192  HCAPLUS
TITLE:                   Long lasting natriuretic peptide
                         derivatives
INVENTOR(S):             Bridon, Dominique P.; Bakis, Peter; Carette,
                         Julie; Leclaire, France; Leger, Roger; Robitaille,
                         Martin
PATENT ASSIGNEE(S):      Conjuchem Inc., Can.
SOURCE:                  PCT Int. Appl., 108 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  3
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011498	A2	20040205	WO 2003-CA1097	20030729

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-400199P P 20020731
US 2002-400413P P 20020731

AB This invention relates to long lasting natriuretic peptide (NP) derivatives. The NP derivative has a NP peptide and a reactive entity coupled to the NP peptide. The reactive entity is able to covalently bond with a functionality on a blood component. In particular, this invention relates to NP derivatives having an extended in vivo half-life, and method for the treatment of cardio-vascular diseases and disorders such as acute decompensated congestive heart failure (CHF) and chronic CHF.

L41 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:99264 HCAPLUS
TITLE: Kringle 5 peptide-albumin conjugates with anti-migratory activity
AUTHOR(S): Leger, Roger; Benquet, Corinne; **Huang, Xicai**; Quraishi, Omar; van Wyk, Pieter; **Bridon, Dominique**
CORPORATE SOURCE: 225 President-Kennedy Ave., Research Department, ConjuChem Inc., Suite 3950, Montreal, QC, H2X 3Y8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 841-845
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three peptide fragments of the kringle 5 region of plasminogen and their resp. N- and C-terminus maleimido derivs. conjugated to Cys34 of human serum albumin were evaluated in vitro using a human umbilical vein endothelial cell (HUVEC) migration assay and a human plasma stability assay. The N-terminus maleimido derivative of the 64 to 74 segment of kringle 5 conjugated to human serum albumin possessed remarkable anti-migratory activity.

L41 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927456 HCAPLUS
DOCUMENT NUMBER: 138:11387
TITLE: Long **lasting** fusion **peptide** inhibitors for HIV infection
INVENTOR(S): Erickson, John; **Bridon, Dominique P.**; Robitaille, Martin; Krafft, Grant A.; Xie, Dong; Afonina, Elena; Liang, Jun; De Meyer, Sandra

PATENT ASSIGNEE(S): Conjuchem Inc., Can.; De Meyer, Sandra
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096935	A2	20021205	WO 2002-CA806	20020531
WO 2002096935	A3	20031002		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-294241P P 20010531
AB The present invention is concerned with This invention relates to C34 peptide derivs. that are inhibitors of viral infection and/or exhibit antifusogenic properties. In particular, this invention relates to C34 derivs. having inhibiting activity against human immunodeficiency virus (HIV), respiratory syncytial virus (RSV), human parainfluenza virus (HPV), measles virus (MeV), and simian immunodeficiency virus (SIV) with long duration of action for the treatment of the resp. viral infections.

L41 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:695985 HCAPLUS
DOCUMENT NUMBER: 137:216938
TITLE: Preparation of polycyclic piperidine derivatives as metalloproteinase inhibitors
INVENTOR(S): De Nanteuil, Guillaume; Benoist, Alain; Lefoulon, Francois; Hickman, John; Pierre, Alain; Tucker, Gordon; **Bridon, Dominique**; Ezrin, Alan; Holmes, Darren; **Huang, Xicai**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Conjuchem Inc.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070521	A1	20020912	WO 2002-FR800	20020306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, TR
FR 2821842 A1 20020913 FR 2001-3068 20010307
FR 2821842 B1 20030509
PRIORITY APPLN. INFO.: FR 2001-3068 A 20010307
OTHER SOURCE(S): MARPAT 137:216938
AB Title compds. I [R, R1 = H, alkyl; R2 = H, OH, NHOH; R3 = (un)substituted Ph, 4-PhC6H4; R4 = group capable of forming a covalent bond with mobile proteins of the blood; R5R6 = atoms required to complete a mono- or bicyclic nitrogen heterocycle; B = bond, alkylene, oxaalkylene thiaalkylene, azaalkylene; m = 0-6; n = 1-6; p = 0, 1] their isomers and their addition salts with a pharmaceutically acceptable acid or a base, were prepared for use as metalloproteinase inhibitors in the treatment of cancer. Thus, the β-carboline II, prepared in a multi-step synthesis, had IC50 87nM for inhibition of MMP-2.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:658156 HCAPLUS
DOCUMENT NUMBER: 137:180207
TITLE: Preparation of long-**lasting** glucagon-like **peptide** 2 (GLP-2) analogs and derivatives for the treatment of gastrointestinal diseases and disorders
INVENTOR(S): **Bridon, Dominique P.**; Boudjellab, Nissab; Leger, Roger; Robitaille, Martin; **Thibaudeau, Karen**; Carette, Julie
PATENT ASSIGNEE(S): Conjuchem Inc., Can.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066511	A2	20020829	WO 2002-CA175	20020215
WO 2002066511	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1360202	A2	20031112	EP 2002-700079	20020215

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-269276P P 20010216
WO 2002-CA175 W 20020215
OTHER SOURCE(S): MARPAT 137:180207
AB This invention relates to glucagon-like peptide 2 (GLP-2) derivs. and analogs with gastrointestinal growth promoting activity that have a reactive entity that makes the peptide capable of bonding to **blood**

component. In particular, this invention relates to GLP-2 peptide derivs. having an extended in vivo half-life, for the treatment or prevention of gastrointestinal disorders or diseases such as inflammatory bowel disease and other gastrointestinal functions, from any segment of the gastrointestinal tract, from the esophagus to the anus.

L41 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:654963 HCAPLUS
DOCUMENT NUMBER: 137:184468
TITLE: Antibodies to argatroban derivatives and their use in therapeutic and diagnostic treatments
INVENTOR(S): **Thibaudeau, Karen**; Blanchard, Dominique; Bridon, Dominique P.; Ezrin, Alan M.; Hardy, Margaret; Boudjellab, Nissab
PATENT ASSIGNEE(S): Conjuchem Inc., Can.
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6440417	B1	20020827	US 1999-434605	19991105

PRIORITY APPLN. INFO.: US 1998-107475P P 19981106
AB Antibodies to a therapeutic agent and its derivs. and conjugates are disclosed, including antibodies to argatroban and its derivs. and conjugates. The antibodies are useful as reagents in assays and diagnostic kits for determining the concentration of a therapeutic agent or its derivs.
and conjugates in biol. samples, and further have therapeutic uses in treatment for potential toxicity associated with stable therapeutic conjugates and derivs., both in vivo and ex vivo. The antibodies may also used in affinity chromatog. separation of diastereoisomers of argatroban and derivs.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:618035 HCAPLUS
TITLE: Dramatic increase in peptide half-life through in vivo bioconjugation to serum albumin
AUTHOR(S): Leger, Roger; Quraishi, Omar; **Thibaudeau, Karen**; L'Archeveque, Benoit; van Wyk, Pieter; Sekhon, Dalbir; Bousquet-Gagnon, Nathalie; Robitaille, Martin; **Huang, Xicai**; Jette, Lucie; Pham, Khan; Lawrence, Betty; Castaigne, Jean-Paul; **Bridon, Dominique**
CORPORATE SOURCE: ConjuChem Inc, Montreal, QC, H2X 3Y8, Can.
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-183. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Serum albumin has been recently identified as a useful carrier protein to

help control distribution and protect potential peptidic drugs from metabolic degradation and clearance while retaining the desired physiol. response. The technol. described herein focuses on the formation of new drug entities derived from known peptides. The activated drug construct (also called Drug Affinity Complex, DAC-) exploits the unique reactivity of the sulfur atom on cysteine 34 of albumin (figure 1) upon intra venous administration, leading to the selective formation of a carbon sulfur bond. The half-lives increase from a few minutes for the native peptides to many hours (18-30 h) for the peptide-albumin conjugates in the rat. Representative results of DAC- derivs. of various clin. relevant peptides (GLP-1, Dynorphin A, Kringle 5) will be presented along with their reactivity toward serum albumin, identification of the conjugate species, improved stability and pharmacokinetics and selectivity of binding to albumin vs. other serum proteins.

L41 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:185625 HCAPLUS
DOCUMENT NUMBER: 134:222561
TITLE: Preparation and formulation of long lasting antineoplastic agents
INVENTOR(S): **Bridon, Dominique P.**; Leger, Roger; **Huang, Xicai**; Milner, Peter G.; Smith, Damon; Ezrin, Alan M.
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017614	A2	20010315	WO 2000-IB1427	20000907
WO 2001017614	A3	20020228		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212120	A2	20020612	EP 2000-962764	20000907
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508502	T2	20030304	JP 2001-521398	20000907

PRIORITY APPLN. INFO.: US 1999-152681P P 19990907
WO 2000-IB1427 W 20000907

OTHER SOURCE(S): MARPAT 134:222561

AB Derivs. of antineoplastic agents, such as A-X-M [A = antitumor agent, such as doxorubicin, taxol, methotrexate, vincristine, tamoxifen, etc.; X = connecting group which includes such subgroups as CO(CH2)2CO, CO(CH2)4CO, CO(CH2)4NH, O(CH2)2O, NH(CH2)2NH, etc.; M = maleimido, succinimidyl] were prepared and formulated for pharmaceutical use as anticancer agents capable of forming covalent bonds with one or more blood components, preferably a mobile blood component. Thus, the dihydrochloride salt of doxorubicin

derivative I [R = NH(CH2)2NHCOCH2O(CH2)2O(CH2)2M, M = maleimido] was prepared in
3 steps starting from doxorubicin and the hydrochloride salt of H2N(CH2)2NHCOCH2O(CH2)2O(CH2)2M (M = maleimido). The prepared agents were tested for their antitumor effect in mice.

L41 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:824301 HCAPLUS
DOCUMENT NUMBER: 134:13338
TITLE: Long **lasting** insulinotropic **peptides**
INVENTOR(S): **Bridon, Dominique P.**; L'Archeveque, Benoit; Ezrin, Alan M.; Holmes, Darren L.; Leblanc, Anouk; St. Pierre, Serge
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069911	A1	20001123	WO 2000-US13563	20000517
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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WO 2000070665	A2	20001123	WO 2000-IB763	20000517
WO 2000070665	A3	20010419		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1171582	A2	20020116	EP 2000-929748	20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1180121	A1	20020220	EP 2000-930796	20000517
EP 1180121	B1	20031022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010750	A	20020226	BR 2000-10750	20000517
AU 754770	B2	20021121	AU 2000-48555	20000517
EP 1264840	A1	20021211	EP 2002-14617	20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003500341	T2	20030107	JP 2000-619018	20000517
JP 2003527312	T2	20030916	JP 2000-618327	20000517

AT 252601	E	20031115	AT 2000-930796	20000517
US 6329336	B1	20011211	US 2000-623618	20000905
US 6514500	B1	20030204	US 2000-657332	20000907
US 2002049153	A1	20020425	US 2001-876388	20010606
US 6593295	B2	20030715		
ZA 2001006676	A	20020719	ZA 2001-6676	20010814
ZA 2001009110	A	20020613	ZA 2001-9110	20011105
NO 2001005584	A	20020103	NO 2001-5584	20011115
US 2003108567	A1	20030612	US 2002-287892	20021104
US 2003108568	A1	20030612	US 2002-288340	20021104

PRIORITY APPLN. INFO.:

US 1999-134406P	P	19990517
US 1999-159783P	P	19991015
US 1999-153406P	P	19990910
EP 2000-932570	A3	20000517
WO 2000-IB763	W	20000517
WO 2000-US13563	W	20000517
US 2000-623618	A3	20000905
US 2000-657332	A3	20000907

AB Modified insulinotropic peptides are disclosed. The modified insulinotropic peptides are capable of forming a peptidase stabilized insulinotropic peptide. The modified insulinotropic peptides are capable of forming covalent bonds with one or more blood components to form a conjugate. The conjugates may be formed in vivo or ex vivo. The modified peptides are administered to treat humans with diabetes and other related diseases.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:824293 HCAPLUS
DOCUMENT NUMBER: 134:17727
TITLE: Long **lasting** fusion **peptide** inhibitors or antiviral agents
INVENTOR(S): **Bridon, Dominique P.**; Dufresne, Robert P.; Boudjellab, Nissab; Robitaille, Martin; Milner, Peter G.
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069902	A1	20001123	WO 2000-US13651	20000517
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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WO 2000070665	A2	20001123	WO 2000-IB763	20000517
WO 2000070665	A3	20010419		

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EP 1171582	A2	20020116	EP 2000-929748	20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1179012	A1	20020213	EP 2000-932570	20000517
EP 1179012	B1	20021023		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010757	A	20020219	BR 2000-10757	20000517
AT 226593	E	20021115	AT 2000-932570	20000517
EP 1264840	A1	20021211	EP 2002-14617	20000517
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JP 2002544287	T2	20021224	JP 2000-618318	20000517
JP 2003500341	T2	20030107	JP 2000-619018	20000517
ES 2185595	T3	20030501	ES 2000-932570	20000517
AU 761591	B2	20030605	AU 2000-50271	20000517
ZA 2001006676	A	20020719	ZA 2001-6676	20010814
ZA 2001009110	A	20020613	ZA 2001-9110	20011105

PRIORITY APPLN. INFO.:
US 1999-134406P P 19990517
US 1999-153406P P 19990910
EP 2000-932570 A3 20000517
WO 2000-IB763 W 20000517
WO 2000-US13651 W 20000517

AB Peptides exhibiting anti-viral and anti-fusogenic activity are modified to provide greater stability and improved half-life in vivo. The selected peptides include fusion inhibitors DP178 and DP107 and related peptides and analogs. The modified peptides are capable of forming covalent bonds with one or more blood components, preferably a mobile blood component.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:824291 HCAPLUS
DOCUMENT NUMBER: 134:21425
TITLE: Protection of endogenous therapeutic peptides from peptidase activity through conjugation to **blood** components
INVENTOR(S): Bridon, Dominique P.; Ezrin, Alan M.; Milner, Peter G.; Holmes, Darren L.; **Thibaudeau, Karen**
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 733 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000069900 A2 20001123 WO 2000-US13576 20000517
WO 2000069900 A3 20010215
WO 2000069900 C2 20020704
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WO 2000070665 A2 20001123 WO 2000-IB763 20000517
WO 2000070665 A3 20010419
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EP 1105409 A2 20010613 EP 2000-936023 20000517
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EP 1171582 A2 20020116 EP 2000-929748 20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
EP 1264840 A1 20021211 EP 2002-14617 20000517
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JP 2003500341 T2 20030107 JP 2000-619018 20000517
JP 2003508350 T2 20030304 JP 2000-618316 20000517
AU 765753 B2 20030925 AU 2000-51393 20000517
US 6514500 B1 20030204 US 2000-657332 20000907
ZA 2001006676 A 20020719 ZA 2001-6676 20010814
ZA 2001009110 A 20020613 ZA 2001-9110 20011105
US 2003108567 A1 20030612 US 2002-287892 20021104
US 2003108568 A1 20030612 US 2002-288340 20021104
PRIORITY APPLN. INFO.: US 1999-134406P P 19990517
US 1999-153406P P 19990910
US 1999-159783P P 19991015
EP 2000-932570 A3 20000517
WO 2000-IB763 W 20000517
WO 2000-US13576 W 20000517
US 2000-657332 A3 20000907

AB A method for protecting a peptide from peptidase activity in vivo, the peptide being composed of between 2 and 50 amino acids and having a C-terminus and an N-terminus and a C-terminus amino acid and an N-terminus amino acid is described. In the first step of the method, the peptide is modified by attaching a reactive group to the C-terminus amino acid, to the N-terminus amino acid, or to an amino acid located between the N-terminus and the C-terminus, such that the modified peptide is capable of forming a covalent bond in vivo with a reactive functionality on a **blood** component. The solid phase peptide synthesis of a number of derivs. with 3-maleimidopropionic acid (3-MPA) is described. In the next step, a covalent bond is formed between the reactive group and a reactive

functionality on a **blood** component to form a peptide-**blood** component conjugate, thereby protecting said peptide from peptidase activity. The final step of the method involves the analyzing of the stability of the peptide-**blood** component conjugate to assess the protection of the peptide from peptidase activity. Thus, the percentage of a K5 kringle peptide (Pro-Arg-Lys-Leu-Tyr-Asp-Lys-NH2) conjugated to human serum albumin via MPA remained relatively constant through a 24-h plasma assay in contrast to unmodified K5 which decreased to 9% of the original amount of K5 in only 4 h in plasma.

L41 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:325963 HCAPLUS
DOCUMENT NUMBER: 130:325398
TITLE: Novel conjugates of RGD-containing peptides and endogenous carriers
INVENTOR(S): Bridon, Dominique P.; Ezrin, Alan M.; Holmes, Darren L.; Krantz, Alexander; **Thibaudeau, Karen**; Blanchard, Dominique
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924462	A2	19990520	WO 1998-US23702	19981106
WO 9924462	A3	19990826		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309205	AA	19990520	CA 1998-2309205	19981106
AU 9913856	A1	19990531	AU 1999-13856	19981106
EP 1028971	A2	20000823	EP 1998-957648	19981106
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JP 2001522863	T2	20011120	JP 2000-520470	19981106
EP 1167383	A1	20020102	EP 2001-121557	19981106
EP 1167383	B1	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1199566	A1	20020424	EP 2001-126379	19981106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2173641	T3	20021016	ES 1998-956656	19981106
AT 235513	E	20030415	AT 2001-121557	19981106

PRIORITY APPLN. INFO.:
US 1997-64705P P 19971107
US 1998-77927P P 19980313
EP 1998-956656 A3 19981106
EP 1998-959387 A3 19981106
WO 1998-US23702 W 19981106

AB Conjugates are prepared from RGD containing peptides, by combining said peptides or analog with a material providing a functionally reactive group capable of reacting with a **blood** component (preferably a mobile **blood** cell or endogenous protein). The conjugates may be administered to patients to provide anti-platelet or anti-adhesion properties through the inhibition of the binding of fibrinogen to the GPIIb/IIIa receptor, and may also be used as probes for receptor activity. The administration to the patient may be made either in vivo or ex vivo and may be performed by either introducing the RGD containing peptide including the reactive functional group into the patient's vascular system or preparing such a conjugate externally and introducing that conjugate to the patient's vascular system. Thus, peptide Ac-RIARGDFPDDRK-NH2 was synthesized using solid-phase methods, and isolated as the tetra-trifluoroacetic acid salt or further derivatized with N-(γ-maleimidobutyryloxy)succinimide or ethylene glycol-bis(succinimidyl-succinate), to give three peptide salts, which were then conjugated to human plasma proteins. In in vivo tests, the three RGD-containing peptide prepns. showed, for example, IC50 values of 5.7-27.61 μM in platelet-poor plasma aggregation tests.

L41 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:547288 HCAPLUS
DOCUMENT NUMBER: 129:288846
TITLE: Shared epitopes of glycoprotein A and protein 4.1 defined by antibody NaM10-3C10
AUTHOR(S): **Rasamoelisolo, M.**; Czerwinski, M.; Willem, C.; Blanchard, D.
CORPORATE SOURCE: Etablissement Transfusion Sanguine de Loire Atlantique/Vendee, Nantes, 44011, Fr.
SOURCE: Hybridoma (1998), 17(3), 283-288
CODEN: HYBRDY; ISSN: 0272-457X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have produced the murine monoclonal antibody (MAb) NaM70-3C10 (IgM) from splenocytes of mice immunized with human red **blood** cells (RBCs). The MAb agglutinated untreated as well as trypsin, chymotrypsin, neuraminidase, or ficin-treated RBCs from controls. In contrast, control RBCs treated with papain or bromelain were not agglutinated. On immunoblots, the MAb bound to glycophorin A (GPA) and to a 80 kDa protein identified as protein 4.1. Anal. by agglutination of variant RBCs carrying hybrid glycophorins made of the N-terminus (amino acids 1-58) of GPA and of the C-terminus (amino acids 27-72) of glycophorin B (GPB) and competition-inhibition test using purified GPA and a synthetic peptide corresponding to the amino acid sequence 48-58 of GPA demonstrated that the epitope is located within residues 48-58 of GPA. Epitope anal. with immobilized peptides showed that the MAb recognizes the sequence 53Pro-Pro-Glu-Glu-Glu58 of GPA. A homologous sequence is also present within amino acids 395 to 405 of protein 4.1. Finally, the MAb bound to 16 kDa chymotryptic peptide of protein 4.1, which carries the above amino acid sequence. In conclusion, it may be assumed that NaM70-3C10 specifically recognizes a common epitope on the extracellular domain of GPA and on the intracellular protein 4.1; this specificity explains the persistence of the 80 kDa band on blots when RBCs are treated with papain.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:763592 HCAPLUS
DOCUMENT NUMBER: 128:21586
TITLE: Comparative study of target antigens for primate xenoreactive natural antibodies in pig and rat endothelial cells
AUTHOR(S): Azimzadeh, Agnes; Wolf, Philippe; **Thibaudeau, Karen**; Cinqualbre, Jacques; Soulillou, Jean-Paul; Anegon, Ignacio
CORPORATE SOURCE: Laboratoire de Chirurgie Experimentale, Fondation Transplantation, Strasbourg, 67200, Fr.
SOURCE: Transplantation (1997), 64(8), 1166-1174
CODEN: TRPLAU; ISSN: 0041-1337
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rat-to-primate cardiac xenograft model has been proposed as an alternative to the clin. relevant but more cumbersome pig-to-primate model for assessing the efficacy of strategies aimed at preventing xenograft hyperacute rejection. As in pig xenografts, the rejection of rat hearts was mediated by the binding of xenoreactive natural antibodies (XNA) and complement activation. The present study was conducted to identify target antigens recognized by cynomolgus and rhesus monkey IgM XNA on rat tissues and cells in comparison with pig cells. The reactivity of rhesus or cynomolgus serum on pig and rat endothelial cells (ECs) was studied by flow cytometry, ELISA, and complement-dependent cytotoxicity, after removal of primate XNA by perfusion of pig livers, immunoadsorption on a Galα(1,3)Gal affinity column, and enzymic removal of α-galactosyl epitopes from the cell surface. Rat and pig EC exts. were also immunopptd. with primate serum and resolved in SDS-PAGE. The expression of the Galα(1,3)Gal epitope was analyzed on rat tissues and ECs by immunohistochem., flow cytometry, and Western blot, using the isolectin B4 from Griffonia simplicifolia. Removal of primate XNA or of αGal epitopes resulted in a decrease in XNA binding to pig and rat cells, leaving a similar degree of residual reactivity in the two species. At least five proteins of 260, 210, 110, 56, and 50 kDa were immunopptd. on rat ECs, with mol. weight similar to several proteins identified on pig ECs. These results suggest that primate XNA recognize similar antigens on rat and pig ECs. Rat cells expressed lower levels of the Galα(1,3)Gal epitope than pig cells. A large proportion, but not all, of primate XNA react with this epitope on pig and rat ECs. This study suggests that the rat is a valuable species for the evaluation of genetic engineering strategies on the vascular endothelium aimed at preventing hyperacute xenograft rejection.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:317205 HCAPLUS
DOCUMENT NUMBER: 126:342242
TITLE: Fine characterization of a series of new monoclonal antibodies directed against glycophorin A
AUTHOR(S): **Rasamoelisolo, M.**; Czerwinski, M.; Bruneau, V.; Lisowska, E.; Blanchard, D.
CORPORATE SOURCE: Etablissement de Transfusion Sanguine de Loire Atlantique/Vendee, Nantes, F-44011, Fr.
SOURCE: Vox Sanguinis (1997), 72(3), 185-191
CODEN: VOSAAD; ISSN: 0042-9007

PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glycophorins A (GPA) and B (GPB) are the major sialoglycoproteins of the human erythrocyte (RBC) membrane. To prepare tools for the anal. of GPA and GPB, we produced a series of new monoclonal antibodies (mAbs) that identified epitopes of GPA. Seven murine monoclonal antibodies directed to glycophorin A (GPA) were fully characterized by agglutination of untreated and enzyme-treated human erythrocytes, inhibition of agglutination using chemical modified glycophorins and peptides from GPA, immunoblotting, and binding to synthetic peptides on plastic pins. The antibodies identify epitopes located on four different portions of GPA: (1) NaM13-6D2 binds to the N-terminal portion of GPA and GPB carrying the N **blood** group antigen; (2) NaM26-3F4 recognizes the homologous portion of GPA and GPB corresponding to their amino acids 6-26; (3) NaM10-2H12, NaM16-IB10 and NaM10-6G4 are specific for the amino acid sequence 38-45 of GPA; and (4) NaM37-5F4 and NaM13-4E4 bind to the amino acid residues 119-124 located on the intracellular portion of GPA. These antibodies represent precise tools to investigate GPA and related mols. in different cells and tissues.

L41 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:323989 HCAPLUS
DOCUMENT NUMBER: 125:7954
TITLE: Characterization of porcine platelet glycoproteins recognized by human natural "anti-Gal" antibodies
AUTHOR(S): **Thibaudeau, Karen**; Borche, Luis; Soulillou, Jean-Paul; Blanchard, Dominique
CORPORATE SOURCE: Cent. Regional Transfusion Sanguine, Nantes, 44011, Fr.
SOURCE: Blood (1996), 87(11), 4636-4642
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human natural "anti-Gal" antibodies are specifically directed Galα1-3Galβ1-4GlcNAc residues expressed on non-primate mammal and new world monkey cells. We investigated the relative involvement of purified IgG and IgM anti-Gal as xenoreactive natural antibodies (XNA). IgG and IgM were isolated from human plasma, and anti-Gal antibodies were purified by affinity chromatog. on a Synsorb-14 column (Chembiomed, Edmonton, Alberta, Canada). Anti-Gal of both IgM and IgG classes represent the bulk of human XNA that bind to porcine platelets in ELISA. On immunoblots, normal human sera, as well as purified IgM and IgG fractions, reacted with 115-, 125-, 135-, 150-, 180-, 210-, and 240-kD pig platelet proteins, whereas purified anti-Gal antibodies of both IgM and IgG classes mainly bound to 135-, 150-, 180-, and 210-kD glycoproteins. A low reactivity was observed in ELISA with anti-Gal free IgM and IgG, indicating that xenoantibodies are not solely directed to galactosyl epitopes. These antibodies revealed bands of 115, 125, and 240 kD. α-Galactosidase treatment of porcine platelet glycoproteins (gps) enriched by affinity chromatog. abrogated the reactivity of 135- and 210-kD proteins. N- and O-glycosidase treatments demonstrated that α-galactosyl residues are located on the O-glycans of the 135-kD component. Finally, glycoproteins of 90 and 135 kD were identified by amino acid sequencing as the pig analogs of the human glycoproteins IIIa and IIb, resp., whereas the 240-kD component was identified as the porcine fibrinogen, using a new murine monoclonal antibody (NaM147-7B6; IgG1)

specific for its β-chain.

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FILE LAST UPDATED: 11 Feb 2004  (20040211/ED)

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L44       17406 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIANGIOGEN?/OBI OR ANTINEOVA
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L50          18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 OR L47


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    FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<


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L57        6241 SEA FILE=WPIX ABB=ON  PLU=ON  ANTIANGIOGEN? OR ANTINEOVASCULAR?
                 OR ?ANGIOGEN? OR ?NEOVASCULAR?
L58       14799 SEA FILE=WPIX ABB=ON  PLU=ON  COVALENT?
L59          17 SEA FILE=WPIX ABB=ON  PLU=ON  L55 AND L56 AND L57
L62           8 SEA FILE=WPIX ABB=ON  PLU=ON  L59 AND L58


=> d que l65
L55      233580 SEA FILE=WPIX ABB=ON  PLU=ON  BLOOD OR PLASMA OR SERUM OR
                LEU!OCYTE# OR ERYTHROCYTE# OR PLATELET? OR ALBUMIN
L56       13414 SEA FILE=WPIX ABB=ON  PLU=ON  ?SUCCINIMID? OR ?MALEIMID?
L57        6241 SEA FILE=WPIX ABB=ON  PLU=ON  ANTIANGIOGEN? OR ANTINEOVASCULAR?
                 OR ?ANGIOGEN? OR ?NEOVASCULAR?
L59          17 SEA FILE=WPIX ABB=ON  PLU=ON  L55 AND L56 AND L57
L63          14 SEA FILE=WPIX ABB=ON  PLU=ON  L59 AND (AMINO OR HYDROXY OR
                THIOL)
L65           1 SEA FILE=WPIX ABB=ON  PLU=ON  L63 AND IMMUNOGENIC/TI


=> s l62 or l65
L76           9 L62 OR L65

=> file biosis confsci biotechno scisearch
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multifile search

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=> d que l71
L66      4893547 SEA BLOOD OR PLASMA OR SERUM OR LEU!OCYTE# OR ERYTHROCYTE# OR
                 PLATELET# OR ALBUMIN
L67        42296 SEA ?SUCCINIMID? OR ?MALEIMID?
L68        81485 SEA ANTIANGIOGEN? OR ANTINEOVASCULAR? OR ?ANGIOGEN? OR
                 ?NEOVASCULAR?
L71           22 SEA L66 AND L67 AND L68


=> dup rem l71
PROCESSING COMPLETED FOR L71
L77           17 DUP REM L71 (5 DUPLICATES REMOVED)
                 ANSWERS '1-9' FROM FILE BIOSIS
                 ANSWERS '10-14' FROM FILE BIOTECHNO
                 ANSWERS '15-17' FROM FILE SCISEARCH

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PROCESSING COMPLETED FOR L50
PROCESSING COMPLETED FOR L77
PROCESSING COMPLETED FOR L76
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remove duplicate records

L78 44 DUP REM L50 L77 L76 (0 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE HCAPLUS
ANSWERS '19-27' FROM FILE BIOSIS
ANSWERS '28-32' FROM FILE BIOTECHNO
ANSWERS '33-35' FROM FILE SCISEARCH
ANSWERS '36-44' FROM FILE WPIX

Remove duplicates from set containing records from all databases searched.

=> d l78 ibib ab 1-
YOU HAVE REQUESTED DATA FROM 44 ANSWERS - CONTINUE? Y/(N):y

L78 ANSWER 1 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:221927 HCAPLUS
DOCUMENT NUMBER: 138:234483
TITLE: Immobilization method and surfaces produced using said method
INVENTOR(S): Oscarsson, Sven; Quist, Arjan; Pavlovic, Elisabeth; Oehman, Ove
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003023402	A1	20030320	WO 2002-SE1635	20020912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2001-3021 A 20010912
AB Objects, such as mols., macromols., nanoparticles, cells and organelles are immobilized to a surface by covalent bonds and in a site-specific manner using an external source of energy, acting on the surface in the presence of said objects, when said surface and said objects have been chemical derivatized to present groups capable of forming reactive moieties when subjected to said source of energy. The exact location of the immobilization is determined either by exposing the surface to said source of energy in a highly localized manner, or by creating site-specific defects or a pattern, to which groups capable of forming reactive moieties when subjected to said source of energy are first arranged. Said pattern may be in the form of electrodes, arranged on the surface. SPDP-modified HSA only bound to 3-MPTMS-derivatized silicon surface when exposed to an elec. current.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 2 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173618 HCAPLUS

DOCUMENT NUMBER: 138:205301
TITLE: Preparation of uronic acid monosaccharide derivatives for treatment of pathological disease associated with FGF activity or as glyco-processing inhibitors
INVENTOR(S): Murphy, Paul Vincent
PATENT ASSIGNEE(S): University College Dublin, Ire.
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018598	A2	20030306	WO 2002-IE126	20020830
WO 2003018598	A3	20031127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
EP 2001-650096 A 20010830
IE 2001-971 A 20011108
IE 2002-258 A 20020409
IE 2002-675 A 20020814

OTHER SOURCE(S): MARPAT 138:205301

AB Uronic acid monosaccharide (pyranoside) conjugates I, were prepared wherein A1 to A3 is any one or more of the same or different of OH; F; or NH2; wherein when B is CO2H, X is NR2CO; NR2COCH2; NR2COCH2O; NR2COCH=CH; NR2COCH2CH2; NR2COCH2CH2CO; NR2SO2CH2, NR2SO2CH2O; NR2SO2CH=CH; NR2SO2CH2CH2; NR2SO2CH2CH2CO; CONR2; CONR2CH2; CONR2CH2O; CONR2CH=CH; CONR2CH2CH2; CONR2CH2CH2CO; SO2NR2CH2; SO2NR2CH2O; SO2NR2CH=CH; SO2NR2CH2CH2; or SO2NR2CH2CH2CO; wherein R2 is H or alkyl, and R is benzene; pyridine; pyrazine; thiophene; furan; cyclopropyl; indole; quinoline; naphthalene; chrom-4-enone; or substituted THF, to be useful as enhancers and/or inhibitors of heparin binding to FGF. The compds. have the potential to be useful in regenerative medicine or for treatment of pathol. disease associated with FGF activity or as glyco-processing inhibitors. In particular the compds. are potential modulators of fibroblast growth factors (FGFs) and fibronectin, as mitogenic agents and as inhibitors of endothelial cell survival. Thus, I (X = NH, R = COCHMeCH2CH2Me, A1-A3 = OH, B = CO2H) was prepared and tested in vitro for treatment of pathol. disease associated with FGF activity or as glyco-processing inhibitors.

L78 ANSWER 3 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:376312 HCAPLUS
DOCUMENT NUMBER: 138:365138
TITLE: Particles for immunoassays and methods for treating the same
INVENTOR(S): Lawrence, Christopher C.; Yuan, Wei; Shanafelt, Armen B.
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003092201	A1	20030515	US 2001-53058	20011102
US 2003087458	A1	20030508	US 2001-25196	20011218
EP 1319953	A1	20030618	EP 2002-24080	20021029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2003185667	A2	20030703	JP 2002-318893	20021031

PRIORITY APPLN. INFO.: US 2001-53058 A2 20011102
US 2001-25196 A 20011218
OTHER SOURCE(S): MARPAT 138:365138
AB A method of treating particles to be used in immunoassays reduces interference in particle agglutination assays. For particles having covalently bound antibodies and residual NHS-ester or sNHS-ester groups on the surface, the reactive esters are treated with an aqueous mixture containing an amine compound of formula (I): H2N-R-X. The moiety -X is -NH2, -OH, or -CO2CH2CH3; and R is an alkyl group or an alkyl ether group. When -X is -NH2 or -CO2CH2CH3, R contains from 1 to 20 carbon atoms; and when -X is -OH, R contains from 4 to 20 carbon atoms.

L78 ANSWER 4 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:355758 HCAPLUS
DOCUMENT NUMBER: 138:350816
TITLE: Particles for immunoassays and methods for treating the same
INVENTOR(S): Lawrence, Christopher C.; Yuan, Wei; Shanafelt, Armen B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 53,058.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087458	A1	20030508	US 2001-25196	20011218
US 2003092201	A1	20030515	US 2001-53058	20011102
EP 1319953	A1	20030618	EP 2002-24080	20021029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2003185667	A2	20030703	JP 2002-318893	20021031

PRIORITY APPLN. INFO.: US 2001-53058 A2 20011102
US 2001-25196 A 20011218
OTHER SOURCE(S): MARPAT 138:350816
AB A method of treating particles to be used in immunoassays reduces interference in particle agglutination assays. For particles having covalently bound antibodies and residual NHS-ester or sNHS-ester groups on

the surface, the reactive esters are treated with an aqueous mixture containing an amine compound of formula (I): 2 The moiety -X is -NH2, -OH, or -CO2CH2CH3; and R is an alkyl group or an alkyl ether group. When -X is -NH2 or -CO2CH2CH3, R contains from 1 to 20 carbon atoms; and when -X is -OH, R contains from 4 to 20 carbon atoms.

L78 ANSWER 5 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:390844 HCAPLUS
DOCUMENT NUMBER: 138:385428
TITLE: Preparation of hydroxamic and carboxylic acid derivatives having MMP and TNF inhibitory activity
INVENTOR(S): Owen, David Alan; Montana, John Gary; Keily, John Fraser; Watson, Robert John; Baxter, Andrew Douglas
PATENT ASSIGNEE(S): Darwin Discovery Ltd., UK
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 209,627, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6566384	B1	20030520	US 2001-11031	20011113
ZA 9707044	A	19980807	ZA 1997-7044	19970807
US 6118001	A	20000912	US 1997-908397	19970807
US 2003207889	A1	20031106	US 2003-425307	20030429

PRIORITY APPLN. INFO.:
GB 1996-16599 A 19960807
GB 1997-7427 A 19970411
US 1997-908397 A1 19970807
US 1998-209627 B2 19981211
US 2001-11031 A1 20011113

OTHER SOURCE(S): MARPAT 138:385428

AB Hydroxamic and carboxylic acid derivs. of general formula B-SO2-CH2-CHR1-CO-NHOH [wherein R1 = C1-6 alkyl optionally substituted with R9; B = C1-6 alkyl substituted with OR6; R6 = C1-4 alkyl, aryl, C1-6 alkylaryl, heteroaryl, C1-6 alkylheteroaryl, cycloalkyl, C1-6 alkyl-cycloalkyl, heterocycloalkyl, C1-6 alkyl-heterocycloalkyl; R6 is optionally substituted with R8, COR8, SO0-2R8, CO2R8, OR8, CONR2R8, NR2R8, halogen, cyano, SO2NR2R8, or NO2, and for each case of N(R6)2 the R6 groups are the same or different or N(R6)2 is heterocycloalkyl optionally substituted with R8, COR8, SO0-2R8, CO2R8, OR8, CONR2R8, NR2R8, halogen, cyano, SO2NR2R8 or NO2; R8 = C1-6 alkyl, aryl, C1-6 alkyl-aryl, heteroaryl, C1-6 alkyl-heteroaryl; R9 = phthalimido, succinimido, and a moiety of the formula Q; wherein R2 = H, C1-6 alkyl] or salts, solvates, hydrates or protected amino or protected carboxy derivs. thereof are prepared These compds. have matrix metalloproteinase (MMP) and tumor necrosis factor (TNF) inhibitory activity and are used for treatment or prevention of a condition associated with matrix metalloproteinases or mediated by TNF-α or enzymes involved in the shedding of L-selectin, the TNF receptors, or IL-6 receptors (no data). The condition includes cancer, inflammation and inflammatory diseases, tissue degeneration, periodontal disease, ophthalmol. disease, dermatol. disorders, fever, cardiovascular effects, hemorrhage, coagulation and acute phase response, cachexia, anorexia, acute infection, HIV infection, shock states, graft vs. host reactions, autoimmune disease, reperfusion injury, meningitis,

migraine, and aspirin-independent antithrombosis. It also includes tumor growth, angiogenesis, tumor invasion and spread, metastases, malignant ascites, malignant pleural effusion, cerebral ischemia, ischemic heart disease, rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, multiple sclerosis, neurodegeneration, Alzheimer's, atherosclerosis, stroke, vasculitis, Crohn's disease and ulcerative colitis, corneal ulceration, retinopathy, surgical wound healing, psoriasis, atopic dermatitis, chronic ulcers and epidermolysis bullosa, periodontitis and gingivitis, rhinitis, allergic conjunctivitis, eczema, anaphylaxis, restenosis, congestive heart failure, endometriosis, atherosclerosis, and endosclerosis. Thus, to a suspension of intermediate 550 mg 2-[3-(4-Chloro-phenoxy)propane-1-sulfonylmethyl]-5-(3,4,4-trimethyl-2,5-dioxoimidazolidin-1-yl)pentanoic acid in 30 mL dry CH2Cl2 under nitrogen was added, 324 mg 1,3-dimethylaminopropyl-3-ethylcarbodiimide, stirred at room temperature for 15 min, treated with 165 mg tert-butyldimethylsilylhydroxylamine, and stirred for 2 h to give, after workup and desilylation with HCl/Et2O, 2-[3-(4-Chlorophenoxy)propanylsulfonylmethyl]-5-(3,4,4-trimethyl-2,5-dioxoimidazolidin-1-yl)pentanoic acid N-hydroxyamide.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 6 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:555500 HCAPLUS
DOCUMENT NUMBER: 137:109373
TITLE: Preparation of serine protease inhibitors comprising a non-peptide boronate or other hydrogen-bond acceptor
INVENTOR(S): Deadman, John Joseph; Spencer, John; Greenidge, Paulette Angela; Goodwin, Christopher Andrew; Kakkar, Vijay Vir; Scully, Michael Finbarr
PATENT ASSIGNEE(S): Trigen Limited, UK
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057273	A1	20020725	WO 2002-GB224	20020118
WO 2002057273	C2	20021128		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-1537 A 20010120
US 2001-267172P P 20010206
OTHER SOURCE(S): MARPAT 137:109373
AB X-Ar-LJ (I; e.g. isothiouronium salts 2-(2-((carbamimidoylthio)methyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane hydrobromide and 3-nitrobenzyl carbamimidothioate hydrobromide) are useful as protease inhibitors. In I,

Ar is a ring or ring system, for example a benzene ring, and may be substituted by one or more moieties in addition to X and LJ; X is a functional group which is a H bond acceptor, e.g. a nitro or boronate group BY1Y2; L is a linker, most preferably (CR5R6)-S-; J is a moiety containing a basic N atom but not containing an amino acid residue, preferably amidino, guanidino, amino, carboxamido, hydroxylamino, or imidazolyl, or an N-substituted analog thereof. Enzyme inhibition activities for some of the claimed compds. for up to 6 enzymes (plasmin, thrombin, trypsin, factor IX, factor X, urokinase) are reported. Several methods of preparation are claimed and 31 prepns. are included.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 7 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:889449 HCAPLUS
DOCUMENT NUMBER: 137:365992
TITLE: **Covalent** modification of abnormal prion protein with polymer for prion inactivation
INVENTOR(S): Scott, Mark D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002172977	A1	20021121	US 2001-861306	20010518
US 6555656	B2	20030429		

PRIORITY APPLN. INFO.: US 2001-861306 20010518

AB A prion-physiol. structure and associated method of formation are presented. A provided abnormal prion has a transforming power over a normal prion to convert the abnormal prion into defective prion that mimics the abnormal prion. A linker mol. is then bonded to the abnormal prion, wherein a polymer that is covalently attached to the linker mol. facilitates formation of a polymerized abnormal prion that does not have the transforming power over the normal prion.

L78 ANSWER 8 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:21026 HCAPLUS
DOCUMENT NUMBER: 136:258547
TITLE: Renal damage, metabolism and **covalent** binding following administration of the nephrotoxicant N-(3,5-dichlorophenyl)**succinimide** (NDPS) to male Fischer 344 rats
AUTHOR(S): Henesey, Caroline M.; Harvison, Peter J.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of the Sciences in Philadelphia, Philadelphia, PA, 19104-4495, USA
SOURCE: Toxicology (2002), 170(3), 187-200
CODEN: TXCYAC; ISSN: 0300-483X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vivo metabolism, nephrotoxicity and covalent binding to proteins were evaluated in male Fischer 344 rats that received [2,3-14C]-N-(3,5-

dichlorophenyl)succinimide (14C-NDPS). Some animals were pretreated with the enzyme inducer phenobarbital (PB, 80 mg/kg per day, for 3 days, i.p. in saline) prior to receiving a non-nephrotoxic dose of 14C-NDPS (0.2 mmol/kg, i.p. in corn oil). Other rats were pretreated with the cytochrome P 450 inhibitor 1-aminobenzotriazole (ABT, 100 mg/kg, 1 h prior to NDPS, i.p. in saline) before administration of a non-toxic or a toxic dose (0.2 or 0.6 mmol/kg, resp., i.p. in corn oil) of 14C-NDPS. Non-pretreated animals received either dose of 14C-NDPS, but did not receive PB or ABT. All rats were sacrificed 6 h after administration of 14C-NDPS. Nephrotoxicity was monitored by measuring urine volume, urine protein concns., blood urea nitrogen levels, and kidney wts. The NDPS metabolic profile in tissue, blood, and urine was analyzed by HPLC. Covalent binding of 14C-NDPS-derived radioactivity to tissue proteins was also measured. Compared with non-pretreated rats, PB-pretreatment potentiated the toxicity of the non-toxic dose of 14C-NDPS. In contrast, ABT-pretreatment protected the rats against NDPS nephrotoxicity. The amount of N-(3,5-dichlorophenyl)-2-hydroxysuccinamic acid (2-NDHSA), an oxidative, nephrotoxic metabolite of NDPS, was elevated in kidney homogenates and urine by PB-pretreatment (0.2 mmol/mg NDPS). ABT pretreatment inhibited NDPS metabolism at both doses. Covalent binding of 14C-NDPS (0.2 mmol/kg)-derived radioactivity to renal and plasma proteins was higher in the PB-pretreated rats than in the non-pretreated animals. In contrast, ABT-pretreatment partially inhibited covalent binding at both doses of 14C-NDPS. These results suggest that there is a relationship between oxidative metabolism of NDPS, covalent binding of an NDPS metabolite to renal proteins, and NDPS-induced nephrotoxicity in rats.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 9 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:581916 HCAPLUS
DOCUMENT NUMBER: 135:175376
TITLE: Ligand for vascular endothelial growth factor receptor
INVENTOR(S): Tchistiakova, Lioudmila; Li, Shengmin; Pietrzynski, Grzegorz; Alakhov, Valery
PATENT ASSIGNEE(S): Supratek Pharma Inc., Can.
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057067	A1	20010809	WO 2001-IB135	20010202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002058619	A1	20020516	US 2001-775743	20010202
EP 1252177	A1	20021030	EP 2001-948985	20010202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003528824 T2 20030930 JP 2001-557898 20010202
PRIORITY APPLN. INFO.: US 2000-180568P P 20000204
WO 2001-IB135 W 20010202
OTHER SOURCE(S): MARPAT 135:175376
AB The present invention relates to compns. comprised of a peptide ligand or derivs. thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivs. thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 10 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:167844 HCAPLUS
DOCUMENT NUMBER: 134:227368
TITLE: Nitric oxide-producing polymeric hydrogel materials
INVENTOR(S): Hill-West, Jennifer L.; Bohl, Kristyn Simcha
PATENT ASSIGNEE(S): Rice University, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015738	A2	20010308	WO 2000-US24058	20000901
WO 2001015738	A3	20020131		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194171	A2	20020410	EP 2000-959750	20000901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-152054P P 19990902
WO 2000-US24058 W 20000901
AB Hydrogels releasing or producing NO, most preferably photopolymerizable biodegradable hydrogels capable of releasing physiol. amts. of NO for prolonged periods of time, are applied to sites on or in a patient in need of treatment thereof for disorders such as restenosis, thrombosis, asthma, wound healing, arthritis, penile erectile dysfunction or other conditions where NO plays a significant role. The hydrogels are typically formed of macromers, which preferably include biodegradable regions, and have bound thereto groups that are released in situ to elevate or otherwise modulate NO levels at the site where treatment is needed. The macromers can form a

homo or hetero-dispersion or solution, which is polymerized to form a hydrogel material, that in the latter case can be a semi-interpenetrating network or interpenetrating network. Compds. to be released can be phys. entrapped, covalently or ionically bound to macromer, or actually form a part of the polymeric material. The hydrogel can be formed by ionic and/or covalent crosslinking. Other active agents, including therapeutic, prophylactic, or diagnostic agents, can also be included within the polymeric material.

L78 ANSWER 11 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:519335 HCAPLUS
DOCUMENT NUMBER: 135:111977
TITLE: Diagnostic/therapeutic agents having phospholipid-based microbubbles coupled to one or more vectors
INVENTOR(S): Klaveness, Jo; Rongved, Pal; Hogset, Anders; Tolleshaug, Helge; Naevestad, Anne; Hellebust, Halldis; Hoff, Lars; Cuthbertson, Alan; Lovhaug, Dagfinn; Solbakken, Magne
PATENT ASSIGNEE(S): Nycomed Imaging As, Norway
SOURCE: U.S., 89 pp., Cont.-in-part of U.S. Ser. No. 958,993.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6261537	B1	20010717	US 1997-960054	19971029
CN 1234742	A	19991110	CN 1997-199047	19971028
US 6331289	B1	20011218	US 1997-959206	19971028
KR 2000052829	A	20000825	KR 1999-703658	19990427
US 2002102215	A1	20020801	US 2001-765614	20010122
US 2002102217	A1	20020801	US 2001-925715	20010810
US 6680047	B2	20040120		
CN 1440816	A	20030910	CN 2002-160420	20021230

PRIORITY APPLN. INFO.:
GB 1996-22366 A 19961028
GB 1996-22367 A 19961028
GB 1996-22368 A 19961028
GB 1997-699 A 19970115
GB 1997-8265 A 19970424
GB 1997-11842 A 19970606
GB 1997-11846 A 19970606
US 1997-49264P P 19970606
US 1997-49265P P 19970606
US 1997-49268P P 19970606
US 1997-958993 A2 19971028
GB 1996-22369 A 19961028
GB 1997-2195 A 19970204
GB 1997-11837 A 19970606
GB 1997-11839 A 19970606
US 1997-49263P P 19970607
US 1997-49266P P 19970607
US 1997-959206 A 19971028
US 1997-960054 A1 19971029

AB Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, having reporters comprise gas-filled

microbubbles stabilized by monolayers of film-forming surfactants, the reporter being coupled or linked to at least one vector. The gas is air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulfur fluoride, selenium hexafluoride, a low mol. weight hydrocarbon, a ketone, an ester, a halogenated low mol. weight hydrocarbon or their mixts. The film-forming surfactant material is one or more phospholipids selected from the group consisting of phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins. A therapeutic agent is an antineoplastic agent, blood product, biol. response modifier, antifungal agent, hormone or hormone analog, vitamin, enzyme, antiallergic agent, tissue factor inhibitor, platelet inhibitor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogenic, circulatory drug, metabolic potentiator, antitubercular, antiviral, vasodilator, antibiotic, anti-inflammatory, antiprotozoal, antirheumatic, narcotic, opiate, cardiac glycoside, neuromuscular blocker, sedative, local anesthetic, general anesthetic or genetic material. For example, an endothelial cell adhesion of phosphatidylserine-encapsulated perfluorobutane microbubbles coated with polylysine was higher than adhesion of uncoated microbubbles. Also, a thrombus was detected by ultrasound in patients with suspected venous thrombosis using i.v. phosphatidylserine-encapsulated microbubbles. The microbubbles contained inactivated human thrombin-succinyl-PEG 3400-distearoylphosphatidylethanol amine incorporated into the encapsulating membrane.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 12 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:795852 HCAPLUS
DOCUMENT NUMBER: 132:34768
TITLE: Divalent antibody fragments
INVENTOR(S): Chapman, Andrew Paul; King, David John
PATENT ASSIGNEE(S): Celltech Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964460	A1	19991216	WO 1999-GB1800	19990608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330186	AA	19991216	CA 1999-2330186	19990608
AU 9942783	A1	19991230	AU 1999-42783	19990608
AU 763246	B2	20030717		
GB 2354242	A1	20010321	GB 2000-30176	19990608
GB 2354242	B2	20031105		
EP 1090037	A1	20010411	EP 1999-955481	19990608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
DE 19983347 T 20010628 DE 1999-19983347 19990608
JP 2002517515 T2 20020618 JP 2000-553466 19990608
PRIORITY APPLN. INFO.: GB 1998-12545 A 19980610
WO 1999-GB1800 W 19990608

AB Divalent antibody fragments are described, each of which has one or more interchain bridges containing a synthetic or naturally occurring polymer selected from a polyalkylene, polyalkenylene, polyoxyalkylene or polysaccharide. Each bridge may be the residue of a homo- or heterobifunctional crosslinking reagent and serves to link two heavy chains in each antibody fragment via the sulfur atoms of cysteine residues present in the chains. Each fragment may be attached to one or more effector or reporter mols., and is of use in therapy or diagnostics where it has markedly improved binding and/or pharmacokinetic properties when compared to other antibody fragments which have the same number and type of polymer mols. but in which the polymer mols. are randomly attached. The antibody fragment is selective to cell surface antigen, e.g. human TNFα, PDGF, or a receptor thereof.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 13 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:271331 HCAPLUS
DOCUMENT NUMBER: 130:311803
TITLE: Preparation of aminobutanoic acid derivatives as inhibitors of matrix metalloproteinases
INVENTOR(S): Takahashi, Kanji; Sugiura, Tsuneyuki
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 557 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919296	A1	19990422	WO 1998-JP4529	19980907
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1024134	A1	20000802	EP 1998-947771	19980907
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 3155536	B2	20010409	JP 2000-515869	19980907
ZA 9809113	A	19990414	ZA 1998-9113	19981006
CA 2305463	AA	19990422	CA 1998-2305463	19981007
AU 9894580	A1	19990503	AU 1998-94580	19981007
AU 760181	B2	20030508		
BR 9812807	A	20001017	BR 1998-12807	19981007
JP 2001172245	A2	20010626	JP 2000-322746	19981007
JP 3470692	B2	20031125		
NZ 503789	A	20021126	NZ 1998-503789	19981007
JP 2003212831	A2	20030730	JP 2002-344969	19981007

RU 2215735	C2	20031110	RU 2000-111472	19981007
NO 2000001813	A	20000609	NO 2000-1813	20000407
MX 200003465	A	20001113	MX 2000-3465	20000407
US 6420427	B1	20020716	US 2000-529056	20000407

PRIORITY APPLN. INFO.: JP 1997-291834 A 19971009
JP 1998-28533 A 19980210
JP 2000-515869 A3 19980907
WO 1998-JP4529 W 19980907
JP 2000-322746 A3 19981007

OTHER SOURCE(S): MARPAT 130:311803

AB Aminobutanoic acid derivs. represented by general formula (I) and salts thereof [wherein R1 = CO2R10, CONHOR10, CONHNHR10, (CH2)nSR50, Y-P(:O)(OR51)2; R10 = H, C1-8 alkyl, Ph, phenyl- or C1-8 alkoxy-C1-8 alkyl, PhO2C, PhCH2O2C, C1-8 alkoxycarbonyl; wherein n = 0-3; R50 = H, C1-8 alkyl, C1-8-alkyl-carbonyl, PhCO, SH, C1-8 alkylthio, SPh; R51 = H, C1-8 alkyl, Ph; Y = single bond, CH2, O; R2-R7 = H, C2-8 alkenyl, (un)substituted SH, OH, or NH2, CO2H, C1-8 alkyl-carbonyl, C1-8 alkoxy-carbonyl, (un)substituted carbocyclyl or heterocyclyl, (un)substituted C1-8 alkyl or C2-8 alkenyl; or R3 and R4 or R5 and R6 together represents C1-8 alkylene; or R2 and R3, R4 and R5, or R6 and R7 together represent C2-8 alkylene; when R8 = H, (un)substituted C1-8 alkyl, or C1-8 alkoxy-carbonyl, R9 = (un)substituted carbocyclyl; or when R8 = (un)substituted carbocyclyl or heterocyclyl, R9 = (un)substituted C1-8 alkyl or C1-8 alkoxy, (un)substituted carbocyclyl; M = C1-8 alkylene; J = single bond, O, S, NH, C1-8 alkyl-N] are prepared and claimed. Also claimed are matrix metalloproteinases containing I as the active ingredients and drugs containing I as the active ingredients for the prevention and/or treatment of rheumatism, osteoarthritis, pathol. bone resorption, osteoporosis, periodontal diseases, interstitial nephritis, arteriosclerosis, pulmonary emphysema, hepatic cirrhosis, corneal injury, diseases due to metastasis and infiltration of cancer cells or proliferation thereof, autoimmune diseases (such as Crohn's disease and Sjogren's disease), diseases due to transmigration of white blood cells or infiltration thereof, neovascularization, multiple sclerosis, aortic aneurysm, or endometritis. For example, the title compound (II) showed IC50 of 26 nM against human stromelysin. A table and an ampule formulation containing II were described.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 14 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:268485 HCAPLUS
DOCUMENT NUMBER: 128:321931
TITLE: Preparation of heteroaryl succinamides as metalloproteinase inhibitors
INVENTOR(S): Bender, Steven L.; Castelhano, Arlindo L.; Chong, Wesley K. M.; Abreo, Melwyn A.; Billedeau, Roland J.; Chen, Jian Jeffrey; Deal, Judith G.
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA; Syntex (U.S.A.) Inc.
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9817643 A1 19980430 WO 1997-US17809 19971006
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
US 6008243 A 19991228 US 1997-823962 19970325
AU 9748060 A1 19980515 AU 1997-48060 19971006
AU 735194 B2 20010705
EP 937042 A1 19990825 EP 1997-910770 19971006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
CN 1233237 A 19991027 CN 1997-198705 19971006
BR 9713278 A 19991103 BR 1997-13278 19971006
JP 2000511201 T2 20000829 JP 1998-519394 19971006
ZA 9709406 A 19980709 ZA 1997-9406 19971021
NO 9901922 A 19990422 NO 1999-1922 19990422
MX 9903730 A 20000228 MX 1999-3730 19990422
US 6174915 B1 20010116 US 1999-309602 19990511
US 6306892 B1 20011023 US 2000-598208 20000621
US 2002019429 A1 20020214 US 2001-922206 20010806
US 6495699 B2 20021217
AU 763835 B2 20030731 AU 2001-78253 20011005
PRIORITY APPLN. INFO.: US 1996-29115P P 19961024
US 1997-823962 A 19970325
AU 1997-48060 A3 19971006
WO 1997-US17809 W 19971006
US 1999-309602 A3 19990511
US 2000-598208 A1 20000621
OTHER SOURCE(S): MARPAT 128:321931
AB The present invention is directed to title compds. I [X = bond, (un)branched, (un)saturated C1-6 alkyl optionally containing O or S atoms, and optionally substituted by F; Y = bond, CH(OH), CO; R1 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = any group R1, COR10; R3 = any group R1, NR11R12, OR11; or R2R3 form cycloalkyl or heterocycloalkyl group; R4 = H, suitable organic moiety; R5 = CONHOH, CO2R13, SH, N(OH)CHO, SCOR14, P(O)(OH)R15, P(O)(OH)OR13; R11 = any group R1, alkoxy; R12 = any group R1; NR12R12 = heteroaryl, heterocycloalkyl; R13 = H, alkyl, aryl; R14 = alkyl, aryl; R15 = alkyl; Q = 5-membered heteroaryl ring containing 1-3 heteroatoms O, S, N] and pharmaceutically acceptable salts and solvates thereof, and pharmaceutically acceptable prodrugs thereof. Compds. I are useful for inhibiting the activity of a metalloproteinase by contacting the metalloproteinase with an effective amount of the inventive compds. Thus, cyclocondensation of Boc-D-Asp(OCH2Ph)-L-Pheol (Boc = Me3CO2C; Pheol = phenylalaninol) (preparation given) with 3-(4-biphenylyl)2,5-dimethoxytetrahydrofuran (preparation given) and catalytic hydrogenolysis gave pyrrole analog II. II and .apprx.60 related heterocycles were tested for inhibitory activity against a variety of metalloproteinases.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 15 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:993310 HCAPLUS
DOCUMENT NUMBER: 124:146389
TITLE: **Covalent** and Selective Labeling of Proteins

with Heavy Metals. Synthesis, x-ray Structure, and Reactivity Studies of N-**Succinimidyl** and N-Sulfosuccinimidyl Ester Organotungsten Complexes

AUTHOR(S): Gorfti, Abdelaziz; Salmain, Michele; Jaouen, Gerard; McGlinchey, Michael J.; Bennouna, Abdelaziz; Mousser, Abdelhamid

CORPORATE SOURCE: Ecole Nationale Superieure de Chimie de Paris, CNRS, Paris, F-75231, Fr.

SOURCE: Organometallics (1996), 15(1), 142-51
CODEN: ORGND7; ISSN: 0276-7333

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 124:146389

AB New functionally substituted η5-cyclopentadienyl and 2-oxaallyl (η1-enolate) W complexes bearing an N-succinimidyl or an N-sulfosuccinimidyl ester were prepared and fully characterized. The mol. structures of [η5-((succinimidooxy)carbonyl)cyclopentadienyl]methyltricarbonyltungsten(II) (2) and [η5-((succinimidooxy)carbonyl)cyclopentadienyl]iodotricarbonyltungsten(II) (5) were solved by x-ray crystallog. The reactivity of these activated esters, I (R = Me, I; R1 = H, SO3-) toward a range of amines and amino acids was studied. While the N-succinimidyl ester enolate is unreactive, N-succinimidyl-substituted cyclopentadienyl complexes were quite reactive, leading to the expected stable organometallic amides II (R = Me, I; R2 = CH2Ph, CH2CH2CO2H). Bovine serum albumin (BSA), a 66 kDa mol. mass globular protein, could be labeled with fair yields, and conjugates were characterized by IR spectroscopy of the CO ligands. Organotungsten N-succinimidyl esters thus appear as promising reagents for the labeling of proteins with heavy metals.

L78 ANSWER 16 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:160326 HCAPLUS

DOCUMENT NUMBER: 110:160326

TITLE: **Covalent** modification of **serum** transferrin with phospholipid and incorporation into liposomal membranes

AUTHOR(S): Afzelius, Pia; Demant, Erland J. F.; Hansen, Gert H.; Jensen, Peter Buhl

CORPORATE SOURCE: Panum Inst., Univ. Copenhagen, Copenhagen, DK-2200, Den.

SOURCE: Biochimica et Biophysica Acta (1989), 979(2), 231-8
CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method is described for incorporation of H2O-soluble proteins into liposomal membranes using covalent protein-phospholipid conjugates in detergent solution A disulfide derivative of phosphatidylethanolamine containing a reactive N-hydroxysuccinimide ester group was prepared, and the derivative allowed to react with serum transferrin in deoxycholate-containing buffer. Disulfide-linked transferrin-phosphatidylethanolamine conjugates containing up to 6 mol phospholipid/mol protein were prepared The amphiphilic conjugates showed solubility properties very similar to integral membrane proteins. The conjugates self-associate to form protein micelles of narrow size distribution (Stokes radii 6-7 nm), and in the presence of excess phospholipid (egg phosphatidylcholine), they readily incorporate into liposomal membranes upon removal of detergent. Stable incorporation into

liposomes requires the introduction of 2 mols. of phosphatidylethanolamine into the transferrin. Using the disulfide linker to release transferrin from the liposomes, evidence is presented for a function of the phosphatidylethanolamine as an anchor-mol. into the liposomal lipid. Optimal conditions for preparation of homogeneous liposomes with diams. in the range 30-125 nm and with a varying content of transferrin are defined. The liposomes appear well suited for studies on liposome-cell membrane interactions.

L78 ANSWER 17 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:557600 HCAPLUS
DOCUMENT NUMBER: 101:157600
TITLE: **Covalent** binding of antibodies to liposomes using a novel lipid derivative
AUTHOR(S): Goundalkar, Ashok; Ghose, Tarun; Mezei, Michael
CORPORATE SOURCE: Fac. Health Profess., Dalhousie Univ., Halifax, NS, B3H 3J5, Can.
SOURCE: Journal of Pharmacy and Pharmacology (1984), 36(7), 465-6
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-[3-(2-Pyridyldithio)propionyl]stearylamine (I) [92279-65-7] was prepared from stearylamine [124-30-1] and the heterobifunctional reagent, N-succinimidyl 3-(2-pyridyldithio)propionate [68181-17-9]. Use of I to covalently couple antibodies to liposomes was investigated. The binding efficiency was 24-32%. The antibodies bound to liposomes retained the specific antibody activity. This new procedure of coupling antibodies to liposomes is be an efficient means to deliver drugs to selected target organs, especially in cancer chemotherapy.

L78 ANSWER 18 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:582140 HCAPLUS
DOCUMENT NUMBER: 93:182140
TITLE: A solid support for affinity chromatography that **covalently** binds thiol groups via a cleavable connector arm
AUTHOR(S): Singh, Pratap; Lewis, Sidney D.; Shafer, Jules A.
CORPORATE SOURCE: Dep. Biol. Chem., Univ. Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Archives of Biochemistry and Biophysics (1980), 203(2), 774-9
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Preparation of an agarose derivative (MPE-agarose) containing a maleimido group which
is attached to agarose via a cleavable Ph ester linkage is described. MPE-agarose reacts with the thiol groups in glutathione, bovine serum albumin, bovine Hb, and yeast and rabbit muscle glyceraldehyde 3-phosphate dehydrogenase. Treatment of the resulting agarose-linked compds. for 10 min with 1M hydroxylamine (pH 7) resulted in the cleavage of the Ph ester linkage, and release of the maleimido derivative of the compound from the gel. In the case of Hb and glyceraldehyde 3-phosphate dehydrogenase noncovalent interactions between the gel and the released protein lowered the amount of protein which dissolved in the hydroxylamine solution upon cleavage of the Ph ester linkages. Noncovalently absorbed protein could be removed from the gel, however, by washing the gel with 2M guanidine-HCl after treatment

with hydroxylamine. Derivs. of MPE-agarose should prove useful in affinity chromatog. and immunoabsorption where it is difficult to elute material bound to conventional affinity supports.

L78 ANSWER 19 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:582175 BIOSIS
DOCUMENT NUMBER: PREV200300572019
TITLE: IN-VITRO AND IN-VIVO EFFECTS OF TROPONIN I, A CARTILAGE-DERIVED **ANGIOGENESIS** INHIBITOR.
AUTHOR(S): Kern, Beatrice E. [Reprint Author]; Castillo, Carlos Fernandez-del [Reprint Author]; Antoniu, Bozena [Reprint Author]; Balcom., James H. [Reprint Author]; Warshaw, Andrew L. [Reprint Author]
CORPORATE SOURCE: Boston, MA, USA
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 326. e-file. Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Introduction: **Antiangiogenesis** agents have promise in initiating cancer implantation and growth. Troponin I is an **antiangiogenic** compound derived from cartilage. Its functional segment resides at amino-acid 96-116. We studied the effects of this peptide (pTnI) on a) endothelial cell tube (capillary progenitor) formation, b) endothelial cell division, c) induction of intercellular adhesion molecule-1 (ICAM-1) by pancreatic cancer cells (CAPAN-1) and d) growth of pancreatic cancer liver metastases in the mouse. Methods: a) Human vascular endothelial cells (HUVEC) were seeded on a basement membrane matrix, incubated with graded concentrations of pTnI, and tube formation was evaluated histologically. b) HUVEC were labeled with carboxyfluorescein diacetate **succinimidyl** ester (CFDA,SE), incubated +/- pTnI, and fluorescence measured at 96 hours by flow cytometry to determine cell division. c) ICAM-1 expression was measured by flow cytometry on HUVEC incubated with CAPAN-1 and treated +/- pTnI. d) CAPAN-1 cells were injected into the spleen of nude mice pre-treated with 3.5 mg/kg/day of pTnI, and body weight, liver weight and tumor burden were measured at 6 weeks. Results: a) pTnI inhibited endothelial cell tube formation ($p<0.0001$) at concentrations as low as 1pg/ml. b) Endothelial cell division was inhibited significantly at 96 hours by 3mg/ml pTnI ($p=0.0001$). c) Supernatant from CAPAN-1 cells upregulated ICAM-1 on HUVEC by 96%. This upregulation was diminished by pre-incubation of CAPAN-1 cells with less than 10ng/ml pTnI ($p<0.01$). d) Mice treated with pTnI had fewer liver metastases compared to controls (liver/body weight 5.5% versus 11.1%, $p<0.05$). Conclusion: The peptide 94-123 of Troponin I has an **antiangiogenic** effect in pancreatic cancer. In-vitro it inhibits pre-vessel tube formation, endothelial cell division, and ICAM-1 upregulation by cancer cells, and in-vivo it reduces metastases from pancreatic cancer to the liver in a mouse model..

L78 ANSWER 20 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:111711 BIOSIS
DOCUMENT NUMBER: PREV200200111711
TITLE: Inflammation, immune reactivity, and **angiogenesis** in a severe combined immunodeficiency model of rheumatoid arthritis.
AUTHOR(S): Davis, Laurie S. [Reprint author]; Sackler, Marian; Brezinschek, Ruth I.; Lightfoot, Ellis; Bailey, Jennifer L.; Oppenheimer-Marks, Nancy; Lipsky, Peter E.
CORPORATE SOURCE: Department of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX, 75390-8884, USA
laurie.davis@utsouthwestern.edu
SOURCE: American Journal of Pathology, (January, 2002) Vol. 160, No. 1, pp. 357-367. print.
CODEN: AJPAA4. ISSN: 0002-9440.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2002
Last Updated on STN: 26 Feb 2002

AB Severe combined immunodeficiency (SCID) mice were engrafted with rheumatoid arthritis (RA) synovium and evaluated to determine whether RA synovial morphology and function were maintained in the RA-SCID grafts. The four major components of RA synovitis, inflammation, immune reactivity, **angiogenesis**, and synovial hyperplasia persisted in RA-SCID grafts for 12 weeks. Retention of chronic inflammatory infiltrates was demonstrated by histological evaluation and by immunohistology for CD3, CD20, and CD68. Staining for CD68 also revealed that the grafts had undergone reorganization of the tissue, possibly as a result of fibroblast hyperplasia. Immune and inflammatory components were confirmed by the detection of human immunoglobulins and human interleukin-6 in **serum** samples obtained from grafted animals. Human **blood** vessels were detected by dense expression of CD31. Small vessels persistently expressed the vitronectin receptor, alphavbeta3, a marker of **angiogenesis**. All vessels expressed VAP-1, a marker of activated endothelial cells. Finally, the grafts retained the ability to support immigration by human **leukocytes**, as demonstrated by the functional capacity to recruit adoptively transferred 5- (and -6)-carboxyfluorescein diacetate **succinimidyl** ester-labeled T cells. T cells entering the RA-SCID grafts became activated and produced interferon-gamma, as detected by reverse transcriptase-polymerase chain reaction analysis. These studies demonstrate that the RA-SCID model maintains many of the phenotypic and functional features of the inflamed RA synovium.

L78 ANSWER 21 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:356820 BIOSIS
DOCUMENT NUMBER: PREV200300356820
TITLE: Thrombin Induces **Angiogenesis** in the Chick Chorioallantoic Model.
AUTHOR(S): Caunt, Maresa [Reprint Author]; Huang, Yao-Qi [Reprint Author]; Brooks, Peter C. [Reprint Author]; Karpatkin, Simon [Reprint Author]
CORPORATE SOURCE: Medicine, NYU School of Medicine, New York, NY, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2686. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 18 Sep 2003

AB The role of thrombin in tumor growth and metastasis is well documented: 1) Thrombin binds to tumor cells making them more adhesive (apprx2-3 fold) to **platelets**, fibronectin, von Willebrand factor and microvascular endothelium; 2) Thrombin-treated tumor cells have apprx 2-fold increased growth in vitro; 3) Thrombin-treated tumor cells enhance subcutaneous tumor cell growth 18 fold and experimental pulmonary metastasis (tumor volume) 10-156 fold in vivo. The discrepancy between the fold effect on in vitro adhesion and tumor growth with in vivo growth and metastasis prompted an analysis of the role of **angiogenesis** in thrombin-enhanced tumor cell growth and metastasis. We have recently reported the upregulation of the vascular growth factor VEGF (Thromb Haemost 86:1094, 2001) and Angiopoietin-2 (**Blood** 99:1646, 2002) by thrombin (apprx3-4 fold) and the release of Angiopoietin-1 from **platelets** by thrombin (Thromb Haemost 85:204, 2001). However, direct proof of thrombin induced membrane-associated **angiogenesis** has not been reported. The chick chorioallantoic membrane (CAM) is ideal for this purpose. We first ascertained that thrombin-treated B16 melanoma cells implanted on the CAM increased their tumor volume apprx 2-fold compared to untreated cells at 7 days (n=4), indicating that the model was relevant for independently testing the role of thrombin per se in **angiogenesis**. Ten day old embryo CAMs were incubated with various concentrations of thrombin (0.01-2u/ml) as well as the PAR-1 thrombin receptor activation peptide, SFLLRN (100-300uM), or inhibitors at 24, 48 and 72 hrs at 37degreeC and the membrane removed and analyzed for new **blood** vessel growth. Thrombin enhanced new **blood** vessel growth 2-3 fold with optimum effect at 0.1u/ml, which was inhibited by hirudin (n=10). Similar magnitude results were obtained with 200uM SFLLRN. New vessel growth was completely inhibited by soluble recombinant VEGF and Angiopoietin-1 vascular growth factor receptors, KDR-Fc (25 ng/ml) and Tie-2-Fc (50ng/ml) respectively (n=3). PCR analysis of mRNA extracted from CAM at 72 hrs revealed an upregulation of VEGF mRNA (apprx3-fold) with no effect on other vascular growth factors, bFGF or Angiopoietin-2. Complete inhibition of thrombin-induced **angiogenesis** was also obtained with the G-protein-coupled receptor inhibitor, pertussis toxin (25 ng/egg), the protein kinase C inhibitor, **bisindolylmaleimide** (1um/egg) and the MAP kinase inhibitor, PDC980598 (10um/egg). However, neither the vascular growth factor receptor inhibitors nor the cell signalling inhibitors inhibited control vessel growth. We conclude that: 1) thrombin can independently induce VEGF and new **blood** vessel growth 2-3 fold in the CAM assay, in addition to its enhancing effect on tumor cell growth in vitro; 2) KDR-Fc and Tie-2-Fc, agents which inhibit **neoangiogenesis** and 3 inhibitors of thrombin-induced signalling had no effect on control vascular growth.

L78 ANSWER 22 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:336126 BIOSIS
DOCUMENT NUMBER: PREV200300336126
TITLE: PKC delta Inhibition Induces Cell Death in Thalidomide and Dexamethasone Resistant Multiple Myeloma Cell Lines.
AUTHOR(S): Bahlis, Nizar J. [Reprint Author]; Sawney, Richi [Reprint

Author]; Gerson, Stanton [Reprint Author]
CORPORATE SOURCE: Department of Medicine, Division of Hematology Oncology, Case Western Reserve University, Cleveland, OH, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1526. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 22 Aug 2003

AB Protein Kinase C isoenzymes have been implicated in a variety of cellular disorders with disregulation of cytokines and growth factor signal transduction pathway, in particular, those of VEGF and Interleukin-6. These disregulated pathways appear intimately involved in neoplastic cells survival and migration. However the contribution of Protein Kinase C isoenzymes to **plasma** cell dyscrasia pathogenesis is poorly understood. To evaluate this effect, dexamethasone (dex) sensitive (MM1.S), dex resistant (MM1.R) and dex and Fas resistant (U266) human myeloma cell lines were cultured in the presence or absence of a non-specific PKC inhibitor BIM (**bisindolylmaleimide** I hydrochloride) and viability was assessed by Annexin-V FITC staining and FACScan analysis. BIM treatment (4 muM, 24 hours) significantly decreased the viability of these cell lines regardless of sensitivity to dexamethasone or Fas. We next evaluated the effect of a specific PKCdelta inhibitor, Rottlerin, on the viability of these cells since PKCdelta was recently reported to mediate Interleukin-6 receptor shedding in myeloma cells as well as the **angiogenic** effects of VEGF. Rottlerin treatment (4muM, 24 hours) significantly decreased their viability as measured by Annexin -V staining. Furthermore while MM1.R and U266 cells were resistant to dexamethasone (10 muM, 24 hours) and thalidomide (150 muM, 24 hours) alone, co-treatment with Rottlerin had a synergistic effect. Finally, Rottlerin appears to mediate its effect through both caspase dependent and caspase independent pathways. While Rottlerin induces a significant loss of mitochondrial membrane potential DELTApsiin MM1.S cells (measured with JC-1 probe), the addition of a caspase inhibitor ZVAD-fmk (50muM) only partially inhibited its effect. In summary, PKC delta appears to be a significant downstream signaling target for the induction of apoptosis in multiple myeloma cells even in the presence of dexamethasone and thalidomide resistance.

L78 ANSWER 23 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:322795 BIOSIS
DOCUMENT NUMBER: PREV200100322795
TITLE: The role of vascular endothelial growth factor (VEGF) in the pathophysiology of multiple myeloma (MM).
AUTHOR(S): Podar, Klaus [Reprint author]; Tai, Yu-Tzu [Reprint author]; Sattler, Martin [Reprint author]; Treon, Steven P. [Reprint author]; Mitsiades, Constantine [Reprint author]; Davies, Faith E. [Reprint author]; Lentzsch, Suzanne [Reprint author]; Lin, Boris K. [Reprint author]; Gupta, Deepak [Reprint author]; Hideshima, Teru [Reprint author]; Shima, Yoshihito [Reprint author]; Raje, Noopur [Reprint author]; Chauhan, Dharminder [Reprint author]; Mitsiades,

Nicholas [Reprint author]; Hayashi, Toshiaki [Reprint author]; Anderson, Kenneth C. [Reprint author]
CORPORATE SOURCE: Adult Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 836a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

AB VEGF has an important role in the pathophysiology of solid tumors, and recent studies also suggest a role in the development, maintenance, and progression of hematological malignancies by promoting bone marrow (BM) **angiogenesis**. In this study we characterized the direct action of VEGF on MM cells. We demonstrate that VEGF is produced both by MM cells and bone marrow stromal cells (BMSCs), and that adherence of MM cells to BMSCs triggers increased (3-4 fold) VEGF secretion. VEGF induces modest (2 fold) increments in proliferation, assayed by 3H(dT) uptake, in MM.1S cells and patient MM cells. High-affinity VEGF receptor fms-like tyrosine kinase-1 (Flt-1), but not fetal liver kinase-1 (Flk-1), transcript and protein expression was shown by RT-PCR and immunoprecipitation, respectively, in MM.1S cells. VEGF165, (100ng/ml) triggered specific phosphorylation of ERK in MM.1S, as well as patient MM cells, and patient **plasma** cell leukemia (PCL) cells. Moreover, VEGF induced electric mobility shifting consistent with Raf-1 activation, further supporting ERK signaling mediating proliferation induced by VEGF. Pretreatment of with either anti-human VEGF Ab or the MEK-1 inhibitor PD098059 blocked the proliferative effect of VEGF and further confirmed ERK2 signaling. In contrast, neither the other prominent MAPK pathways (p38, SAPK) nor the STAT3 kinase pathway were activated by VEGF in MM cells. The effect of VEGF on cell migration was next assayed by measuring the transfilter migration activity of MM.1S cells and PCL cells seeded on membranes pre-coated with fibronectin. VEGF (5ng/ml) triggered maximal activation of migration in MM.1S cells (2 fold) and PCL cells (100-fold), which was totally blocked using the protein kinase C (PKC) inhibitor **bisindolylmaleimide** I hydrochloride. These data therefore indicate that VEGF may not only enhance BM **angiogenesis**, but may also enhance proliferation and migration of the MM cells in the BM milieu. Further delineation of VEGF signaling mediating MM cell growth and migration will both enhance our understanding of disease pathogenesis and provide the framework for novel therapeutic strategies.

L78 ANSWER 24 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:521097 BIOSIS
DOCUMENT NUMBER: PREV199900521097
TITLE: Synthesis of (99mTc)ethylenedicysteine-colchicine for evaluation of **antiangiogenic** effect.
AUTHOR(S): Zareneyrizi, Fereshteh; Yang, David J. [Reprint author]; Oh, Chang-Sok; Ilgan, Seyfettin; Yu, Dong-Fang; Tansey, Wayne; Liu, Chun-Wei; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Department of Nuclear Medicine, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX, 77030, USA

SOURCE: Anti-Cancer Drugs, (Aug., 1999) Vol. 10, No. 7, pp. 685-692. print.
CODEN: ANTDEV. ISSN: 0959-4973.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999
Last Updated on STN: 3 Dec 1999

AB **Angiogenesis** is in part responsible for tumor growth and the development of metastasis. Radiolabeled angiongenesis inhibitors would be useful to assess tumor microvasculature density. Colchicine (COL), a potent **antiangiogenic** agent, is known to inhibit microtubule polymerization and cell arrest at metaphase. This study aimed to develop 99mTc-labeled COL (EC-COL) using ethylenedicysteine (EC) as a chelator to assess tumor microvascular density. EC was conjugated to trimethylcolchicinic acid using N-**hydroxysuccinimide** and 1-ethyl-3-dimethylaminopropyl carbodiimide as coupling agents with a yield of 50-60%. In vivo stability was analyzed in rabbit **serum** at 0.5-4 h. Tissue distribution and planar imaging studies of (99mTc)EC-COL were evaluated in breast tumor-bearing rats at 0.5, 2 and 4 h. The data was compared to that using (99mTc)EC (control). The radiochemical yield of (99mTc)EC-COL was greater than 95%. (99mTc)EC-COL was stable in rabbit **serum**. In vivo biodistribution of (99mTc)EC-COL in breast tumor-bearing rats showed increased tumor-to-**blood** (0.52+-0.12 to 0.72+-0.07) and tumor-to-muscle (3.47+-0.40 to 7.97+-0.93) ratios as a function of time. Conversely, tumor-to-**blood** values showed a time-dependent decrease with (99mTc)EC over the same time period. Planar images confirmed that the tumors could be visualized clearly with (99mTc)EC-COL from 0.5 to 4 h. (99mTc)EC-COL may be useful to assess **antiangiogenic** and therapeutic effects during chemotherapy.

L78 ANSWER 25 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:452994 BIOSIS
DOCUMENT NUMBER: PREV199900452994
TITLE: Model for intravital microscopic evaluation of the effects of arterial occlusion-caused ischemia in bone.
AUTHOR(S): Hsieh, A. S.; Winet, H. [Reprint author]; Bao, J. Y.; Stevanovic, M.
CORPORATE SOURCE: Orthopaedic Hospital, 2400 Flower Street, Los Angeles, CA, 90007, USA
SOURCE: Annals of Biomedical Engineering, (July-Aug., 1999) Vol. 27, No. 4, pp. 508-516. print.
CODEN: ABMECF. ISSN: 0090-6964.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999

AB An in vivo model has been developed for chronic observation of the effects of ischemia on cortical bone remodeling and perfused vascularity. Diaphragm occluders were implanted around the right common iliac artery of four rabbits and inflated to produce 10 h of ischemia to the limb. Micro-circulation was monitored with intravital microscopy of injected fluorescent microspheres and FITC-Dextran 70 through a bone window, the tibial bone chamber implant (BCI). Bone resorption and apposition in the BCI were indicated with mineralization dyes. Between 2 and 12 h following release of the occluder, secondary ischemia/no-reflow and other evidence of reperfusion injury were observed. Vessel damage was suggested by abnormally high leakage of FITC-D70 from the few vessels perfused during secondary ischemia. In the weeks following occluder release perfused

vasculature increased beyond pre-occlusion levels. Net bone resorption reached a maximum when vascularity passed normal levels. In order to further validate the arterial occlusion model for osteonecrosis, techniques for (1) confirming bone death and (2) detecting increased **leukocyte** adherence to endothelial cells were added. The dead cell stain Ethidium homodimer-1 was used to tag dead osteocytes immediately after occlusion and produced a measure designated "osteonecrosis index." To detect **leukocytes** adhering to vessel walls, carboxyfluorescein diacetate, **succinimidyl** ester was injected at occluder release. An increase in the number of adherent **leukocytes** was detected.

L78 ANSWER 26 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:111201 BIOSIS
DOCUMENT NUMBER: PREV199191058591; BA91:58591
TITLE: CHARACTERIZATION OF THE RECEPTOR TO VASCULOTROPIN ON BOVINE ADRENAL CORTEX-DERIVED CAPILLARY ENDOTHELIAL CELLS.
AUTHOR(S): PLOUET J [Reprint author]; MOUKADIRI H
CORPORATE SOURCE: INSTITUT NATL DE LA SANTE DE LA RECHERCHE MEDICALE, CENTRE DES CORDELIERS, 15 RUE DE L'ECOLE DE MEDECINE, PARIS, FRANCE
SOURCE: Journal of Biological Chemistry, (1990) Vol. 265, No. 36, pp. 22071-22074.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 27 Feb 1991
Last Updated on STN: 13 Apr 1991

AB Recently a new growth factor was purified to homogeneity, and its bioactivity seemed to be restricted to vascular endothelial derived cells. As it was also **angiogenic** in vivo, it was provisionally named vasculotropin (VAS). As an iodination procedure used to label VAS did not damage the molecule, it was possible to undertake binding studies. The binding of iodinated vasculotropin to bovine adrenal cortex-derived capillary endothelial cells was saturable at 250 PM, and half-maximal binding occurred at 47 PM. Scatchard's analysis of the data demonstrated two apparent classes of binding sites with apparent dissociation constants of 2 and 82 PM displaying 280 and 3400 binding sites, respectively. The binding was specific; half-displacement was observed with a 2-fold excess of unlabeled VAS. The structurally related **platelet**-derived growth factor did not complete in a radioreceptor assay. 125I-VAS was displaced by suramin and not by heparin. 125I-VAS was covalently cross-linked to its cell surface receptor on intact bovine adrenal cortex-derived capillary endothelial cells using the homobifunctional agents ethylene glycol bis(**succinimidyl** succinate) or **disuccinimidyl** tartarate. A major macromolecular species with an apparent molecular mass of 230,000 Da was labeled under reducing and nonreducing conditions. These data demonstrate the existence of a specific binding protein for VAS and an estimation of the size at 185,000 Da.

L78 ANSWER 27 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1987:227294 BIOSIS
DOCUMENT NUMBER: PREV198783115464; BA83:115464
TITLE: INHIBITION OF ENDOTHELIAL CELL PROLIFERATION BY GAMMA INTERFERON.
AUTHOR(S): FRIESEL R [Reprint author]; KOMORIYA A; MACIAG T

CORPORATE SOURCE: LAB MOLECULAR BIOL, JEROME H HOLLAND LAB BIOMED SCI, AM RED CROSS, 15601 CRABBS BRANCH WAY, ROCKVILLE, MD 20855, USA
SOURCE: Journal of Cell Biology, (1987) Vol. 104, No. 3, pp. 689-696.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 22 May 1987
Last Updated on STN: 22 May 1987

AB Endothelial cell growth factor (ECGF) is a potent polypeptide mitogen for endothelial cells and fibroblasts. The mitogenic effects of ECGF are inhibited by the lymphokine gamma-interferon (gamma-IFN) in a dose-dependent manner. Gamma-IFN also induces a unique change in endothelial cell morphology which is maximally expressed in the presence of ECGF. The antiproliferative and phenotypic modulatory effects of gamma-IFN on endothelial cells are reversible. Inhibition of ECGF-induced endothelial cell proliferation by gamma-IFN is accompanied by a concentration- and time-dependent decrease in binding of 125I-ECGF to the endothelial cell surface. Scatchard analyses of the binding data in the presence and absence of gamma-IFN demonstrate a decrease in the number of ECGF-binding sites rather than a decrease in ligand affinity for the receptor. Cross-linking experiments with **disuccinimidyl** suberate demonstrate a decrease in the 170,000 Mr cross-linked receptor-ligand complex. These data suggest that gamma-IFN inhibits endothelial cell proliferation by a mechanism which involves growth factor receptor modulation.

L78 ANSWER 28 OF 44 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36994555 BIOTECHNO
TITLE: **Angiogenesis** in collagen I requires α.sub.2β.sub.1 ligation of a GFP*GER sequence and possibly p38 MAPK activation and focal adhesion disassembly
AUTHOR: Sweeney S.M.; DiLullo G.; Slater S.J.; Martinez J.; Iozzo R.V.; Lauer-Fields J.L.; Fields G.B.; San Antonio J.D.
CORPORATE SOURCE: J.D. San Antonio, Dept. of Medicine, Cardeza Foundation, Thomas Jefferson University, 1015 Walnut St., Philadelphia, PA 19107, United States.
E-mail: james.sanantonio@mail.tju.edu
SOURCE: Journal of Biological Chemistry, (15 AUG 2003), 278/33 (30516-30524), 66 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Angiogenesis** depends on proper collagen biosynthesis and cross-linking, and type I collagen is an ideal **angiogenic** scaffold, although its mechanism is unknown. We examined **angiogenesis** using an assay wherein confluent monolayers of human umbilical vein endothelial cells were overlain with collagen in a **serum**-free defined medium. Small spaces formed in the cell layer by 2 h, and cells formed net-like arrays by 6-8 h and capillary-like lumens by 24 h. Blocking of α.sub.2β.sub.1, but not α.sub.1 or α.sub.vβ.sub.1 integrin function halted morphogenesis. We found that a triple-helical, homotrimeric peptide

mimetic of a putative α.sub.2β.sub.1, binding site: α .sub.1(I)496-507 GARGERGFP*GER (where single-letter amino acid nomenclature is used, P* = hydroxyproline) inhibited tube formation, whereas a peptide carrying another putative site: α.sub.1(I)127-138 GLP*GERGRP*GAP* or control peptides did not. A chemical inhibitor of p38 mitogen-activated protein kinase (p38 MAPK), SB202190, blocked tube formation, and p38 MAPK activity was increased in collagen-treated cultures, whereas targeting MAPK kinase (MEK), focal adhesion kinase (FAK), or phosphatidylinositol 3-kinase (PI3K) had little effect. Collagen-treated cells had fewer focal adhesions and 3- to 5-fold less activated FAK. Thus capillary morphogenesis requires endothelial α.sub.2β.sub.1 integrin engagement of a single type I collagen integrin-binding site, possibly signaling via p38 MAPK and focal adhesion disassembly/FAK inactivation.

L78 ANSWER 29 OF 44 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:35428839 BIOTECHNO
TITLE: Inhibition of the MEK/ERK signaling pathway by the novel antimetastatic agent NAMI-A down regulates c-myc gene expression and endothelial cell proliferation
AUTHOR: Pintus G.; Tadolini B.; Posadino A.M.; Sanna B.; Debidda M.; Bennardini F.; Sava G.; Ventura C.
CORPORATE SOURCE: G. Pintus, Department of Biomedical Sciences, Division of Biochemistry, University of Sassari, Viale San Pietro 43/B, 07100 Sassari, Italy.
E-mail: gpintus@uniss.it
SOURCE: European Journal of Biochemistry, (2002), 269/23 (5861-5870), 42 reference(s)
CODEN: EJBCAI ISSN: 0014-2956
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Imidazolium trans-imidazoledimethyl sulfoxide-tetrachlororuthenate (NAMI-A) is a novel ruthenium-containing experimental antimetastatic agent. Compelling evidence ascribes a pivotal role to endothelial cells in the orchestration of tumor **angiogenesis** and metastatic growth, suggesting **antiangiogenic** therapy as an attractive approach for anticancer treatment. In this context, activation of the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) signaling pathway has been found fundamental in transducing extracellular stimuli that modulate a number of cellular process including cell proliferation, migration and invasion. Here we show that exposure of the transformed endothelial cell line ECV304 to NAMI-A significantly inhibited DNA synthesis, as well as the expression of the proliferating cell nuclear antigene (PCNA). These responses were associated with a marked down-regulation of ERK phosphorylation in **serum**-cultured cells. In addition, NAMI-A markedly reduced **serum** stimulated- and completely suppressed phorbol 12-myristate 13-acetate (PMA)-triggered MAPK/ERK kinase activity. NAMI-A was also able to inhibit the phosphorylation of MEK, the upstream activator of ERK, and, similar to both the protein kinase C (PKC) inhibitor GF109203X and the MAPK/ERK (MEK) inhibitor PD98059, it completely counteracted PMA-induced ERK phosphorylation. Finally, NAMI-A and PD98059 down regulated c-myc gene expression to the same extent in **serum** -cultured cells and dose-dependently counteracted, and ultimately abolished, the increase in c-myc gene expression elicited by PMA in **serum**-free cells. These results suggest that inhibition of

MEK/ERK signaling by NAMI-A may have an important role in modulating c-myc gene expression and ECV304 proliferation.

L78 ANSWER 30 OF 44 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:34920215 BIOTECHNO
TITLE: Significance of vascular endothelial cell growth factor upregulation mediated via a chymase-angiotensin-dependent pathway during **angiogenesis** in hamster sponge granulomas
AUTHOR: Katada J.; Muramatsu M.; Hayashi I.; Tsutsumi M.; Konishi Y.; Majima M.
CORPORATE SOURCE: Dr. J. Katada, PCD Japan, Pharmacia KK, 3-20-2 Nishi-shinjuku, Shinjuku-ku, Tokyo 163-1448, Japan. E-mail: katada@kt.rim.or.jp
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (2002), 302/3 (949-956), 41 reference(s) CODEN: JPETAB ISSN: 0022-3565
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Chymase is a serine protease responsible for local production of angiotensin (Ang) II from its precursor Ang I in several species, including humans, dogs, and hamsters. We have previously reported that chymase facilitates **angiogenesis** in sponge granulation tissues via local production of Ang II. Herein, we report the significance of vascular endothelial growth factor (VEGF) up-regulation mediated by Ang II during **angiogenesis** in hamster sponge granulomas. Treatment of granulation tissues with an anti-VEGF neutralizing antibody or antisense oligomers against VEGF mRNA significantly reduced Ang II-induced **angiogenesis**, supporting a significant role for VEGF during **angiogenesis**. In cultured fibroblasts prepared from granulation tissues, VEGF mRNA was up-regulated in response to Ang II within 2 h and this enhanced expression was abolished in the presence of an Ang II type 1 receptor-selective antagonist, an inhibitor of nuclear factor-KB activation, or an activator protein-1 inhibitor. To study the significance of local production of Ang II by chymase, we examined the effects of chymostatin on in vivo **angiogenesis**. We found that chymostatin markedly inhibited both up-regulation of VEGF mRNA and **angiogenesis** in granulation tissues treated by compound 48/80 or basic fibroblast growth factor. Our results suggest that Ang II directly acts on fibroblasts in granulation tissue to up-regulate VEGF mRNA and thereby induce **angiogenesis**. Furthermore, a chymase-Ang II-VEGF pathway may operate in granulation tissue as the primary mediator of **angiogenesis**.

L78 ANSWER 31 OF 44 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32738130 BIOTECHNO
TITLE: Oxidized low-density lipoprotein downregulates endothelial basic fibroblast growth factor through a pertussis toxin-sensitive G-protein pathway: Mediator Role of **Platelet**-Activating Factor-Like Phospholipids
AUTHOR: Chang P.-Y.; Luo S.; Jiang T.; Lee Y.-T.; Lu S.-C.; Henry P.D.; Chen C.-H.
CORPORATE SOURCE: Dr. C.-H. Chen, MS A-601, Department of Medicine, Baylor College of Medicine, 6565 Fannin, Houston, TX 77030, United States.

E-mail: cchen@bcm.tmc.edu
SOURCE: Circulation, (31 JUL 2001), 104/5 (588-593), 35 reference(s)
CODEN: CIRCAZ ISSN: 0009-7322
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background - Oxidized LDL (oxLDL) inhibits **angiogenesis** in part by downregulating endothelial basic fibroblast growth factor (bFGF). To determine the mechanism of the downregulation, we investigated the signal transduction pathway involving potential phospholipid mediators. Methods and Results - Cultured bovine aortic endothelial cells were incubated with PBS (lipoprotein-free control), LDL, or copper oxLDL under **serum**-free conditions. At 24 hours, oxLDL (50 μg/mL) decreased bFGF mRNA (Northern blot), bFGF protein (Western blot and ELISA), and concomitant DNA synthesis, all by 40% to 50% compared with PBS. LDL had no effect. Pretreating the cells with 100 ng/mL pertussis toxin (PTX) for 18 hours before oxLDL exposure almost completely blocked the inhibitory effects of oxLDL. In contrast, inhibiting other major cellular signal transduction pathways with PD-98059 (mitogen-activated protein kinase kinase inhibitor), HA-1004 (inhibitor of cGMP- and cAMP-dependent protein kinase), or Ro-31-8220 (protein kinase C inhibitor) or chelating intracellular Ca.sup.2.sup.+ with BAPTA-AM failed to attenuate any of the oxLDL effects assayed. Addition to the cultures of WEB 2086, a specific antagonist of the PTX-sensitive G protein-coupled **platelet** -activating factor (PAF) receptor, blocked the action of oxLDL. Whereas PAF dispersed in the culture medium failed to produce oxLDL-like effects, degradation of PAF and PAF-like phospholipids accumulated in oxLDL with a recombinant human PAF acetylhydrolase eliminated the inhibitory effects of oxLDL on bFGF expression and DNA synthesis. Conclusions - OxLDL suppresses endothelial bFGF expression and DNA synthesis through a PTX-sensitive heterotrimeric G-protein pathway involving mediator phospholipids similar, but not identical, to PAF.

L78 ANSWER 32 OF 44 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1998:28227518 BIOTECHNO
TITLE: Tissue factor-dependent vascular endothelial growth factor production by human fibroblasts in response to activated factor VII
AUTHOR: Ollivier V.; Bentolila S.; Chabbat J.; Hakim J.; De Prost D.
CORPORATE SOURCE: Dr. D. De Prost, Serv. d'Hematologie et d'Immunologie, Hopital Bichat, 46 rue Henri Huchard, 75018 Paris, France.
E-mail: dominique.deprost@bch.ap-hop-paris.fr
SOURCE: Blood, (15 APR 1998), 91/8 (2698-2703), 31 reference(s)
CODEN: BLOOAW ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The transmembrane protein tissue factor (TF) is the cell surface receptor for coagulation factor VII (FVII) and activated factor VII (FVIIa). Recently, TF has been identified as a regulator of **angiogenesis** , tumor growth, and metastasis. This study was designed to link the binding of FVII(a) to its receptor, TF, with the subsequent triggering of

angiogenesis through vascular endothelial growth factor (VEGF) production by human lung fibroblasts. We report that incubation of fibroblasts, which express constitutive surface TF, with FVII(a) induces VEGF synthesis. FVII(a)- induced VEGF secretion, assessed by a specific enzyme-linked immunosorbent assay, was time- and concentration-dependent. VEGF secretion was maximal after 24 hours of incubation of the cells with 100 nmol/L FVII(a) and represented a threefold induction of the basal VEGF level. Reverse transcriptase-polymerase chain reaction analysis of VEGF detected three mRNA species of 180,312, and 384 bp corresponding, respectively, to VEGF.sub.1.sub.2.sub.1, VEGF.sub.1.sub.8.sub.6, and VEGF.sub.1.sub.8.sub.9. A 2.5- to 3.5-fold increase was observed for the 180- and 312-bp transcripts at 12 and 24 hours, respectively. FVII(a)-dependent VEGF production was inhibited by a pool of antibodies against TF, pointing to the involvement of this receptor. On specific active-site inhibition with dansyl-glutamyl-glycinyl-arginyl chloromethyl ketone, FVIIa lost 70% of its capacity to elicit VEGF production. Consistent with this, the native form (zymogen) of FVII only had a 1.8-fold stimulating effect. Protein tyrosine kinase and protein kinase C are involved in signal transduction leading to VEGF production, as shown by the inhibitory effects of genistein and GF 109203X. The results of this study indicate that TF is essential for VIIa-induced VEGF production by human fibroblasts and that its role is mainly linked to the proteolytic activity of the TF-VIIa complex.

L78 ANSWER 33 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:608330 SCISEARCH
THE GENUINE ARTICLE: 574FQ
TITLE: Cytotoxic targeting of F9 teratocarcinoma tumours with anti-ED-B fibronectin scFv antibody modified liposomes
AUTHOR: Marty C; Odermatt B; Schott H; Neri D; Ballmer-Hofer K; Klemenz R; Schwendener R A (Reprint)
CORPORATE SOURCE: Univ Zurich, Inst Med Radiobiol, CH-5232 Villigen, Switzerland (Reprint); Paul Scherrer Inst, CH-5232 Villigen, Switzerland; Univ Zurich Hosp, Dept Pathol, CH-8091 Zurich, Switzerland; Univ Tubingen, Inst Organ Chem, D-72076 Tubingen, Germany; Swiss Fed Inst Technol, Dept Appl Biosci, CH-8057 Zurich, Switzerland
COUNTRY OF AUTHOR: Switzerland; Germany
SOURCE: BRITISH JOURNAL OF CANCER, (1 JUL 2002) Vol. 87, No. 1, pp. 106-112.
Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0007-0920.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We prepared small unilamellar liposomes derivatised with single chain antibody fragments specific for the ED-B domain of B-fibronectin, This extracellular matrix associated protein is expressed around newly forming **blood** vessels in the vicinity of many types of tumours. The single chain antibody fragments were functionalised by introduction of C-terminal cysteines and linked to liposomes via **maleimide** groups located at the terminal ends of poly(ethylene glycol) modified phospholipids. The properties of these anti-ED-B single chain antibody fragments-liposomes were analysed in vitro on ED-B fibronectin expressing Caco-2 cells and in vivo by studying their biodistribution and their therapeutic potential in mice bearing subcutanous F9 teratocarcinoma tumours. Radioactively

labelled ((114m)Indium) single chain antibody fragments-liposomes accumulated in the tumours at 2-3-fold higher concentrations during the first 2 h after i.v. injection compared to unmodified liposomes. After 6-24 h both liposome types were found in similar amounts (8-10% injected dose g(-1)) in the tumours. Animals treated i.v. with single chain antibody fragments-liposomes containing the new cytotoxic agent 2'-deoxy-5-fluorouridylyl-N-4-octadecyl-1-beta-D-arabinofuranosylcytosine (30 mg kg(-1) per dose, five times every 24 h) showed a reduction of tumour growth by 62-90% determined on days 5 and 8, respectively, compared to animals receiving control liposomes. Histological analysis revealed a marked reduction of F9 tumour cells and excessive deposition of fibronectin in the extracellular matrix after treatment with single chain antibody fragments-2-dioxy-5-fluorouridylyl-N-4-octadecyl-1-beta-D-arabinofuranosylcytosine-liposomes. Single chain antibody fragments-liposomes targeted to ED-B fibronectin positive tumours therefore represent a promising and versatile novel drug delivery system for the treatment of tumours. (C) 2002 Cancer Research UK.

L78 ANSWER 34 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:669713 SCISEARCH
THE GENUINE ARTICLE: PM439
TITLE: COMPARISON OF AMINO-ACID ANALYSES BY PHENYLISOTHIOCYANATE AND 6-AMINOQUINOLYL-N-**HYDROXYSUCCINIMIDYL** CARBAMATE PRECOLUMN DERIVATIZATION
AUTHOR: STRYDOM D J (Reprint); COHEN S A
CORPORATE SOURCE: HARVARD UNIV, SCH MED, CTR BIOCHEM & BIOPHYS SCI & MED, BOSTON, MA, 02115 (Reprint); HARVARD UNIV, SCH MED, DEPT PATHOL, BOSTON, MA, 02115; MILLIPORE CORP, WATERS DIV, MILFORD, MA, 01757
COUNTRY OF AUTHOR: USA
SOURCE: ANALYTICAL BIOCHEMISTRY, (OCT 1994) Vol. 222, No. 1, pp. 19-28.
ISSN: 0003-2697.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB An extensive retrospective comparison was conducted of the long-term repeatability and consistency of amino acid analyses using phenylisothiocyanate and 6-aminoquinolyl-N-**hydroxysuccinimidyl** carbamate (AQC) precolumn derivatization. Amino acid standards were analyzed more than 130 times on more than 60 independent occasions by each of these two precolumn derivatization methodologies, during routine amino acid analysis procedures. Similar coefficients of variation were seen only when very freshly prepared derivatives were analyzed. When realistic aging for <20 h was taken into account, the extreme stability of the AQC derivatives stood out. Chromatography of AQC derivatives using HPLC solvents prepared on a large scale provided the lowest coefficients of variation. The superiority of AQC over PTC methodology was clearly apparent. (C) 1994 Academic Press, Inc.

L78 ANSWER 35 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:6977 SCISEARCH
THE GENUINE ARTICLE: EP556
TITLE: CHARACTERIZATION OF THE RECEPTOR TO VASCULOTROPIN ON BOVINE ADRENAL CORTEX-DERIVED CAPILLARY ENDOTHELIAL-CELLS
AUTHOR: PLOUET J (Reprint); MOUKADIRI H

CORPORATE SOURCE: INSERM, CTR CORDELIERS, 15 RUE ECOLE MED, F-75005 PARIS, FRANCE (Reprint)
COUNTRY OF AUTHOR: FRANCE
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1990) Vol. 265, No. 36, pp. 22071-22074.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recently a new growth factor was purified to homogeneity, and its bioactivity seemed to be restricted to vascular endothelial derived cells. As it was also **angiogenic** in vivo, it was provisionally named vasculotropin (VAS). As an iodination procedure used to label VAS did not damage the molecule, it was possible to undertake binding studies. The binding of iodinated vasculotropin to bovine adrenal cortex-derived capillary endothelial cells was saturable at 250 pM, and half-maximal binding occurred at 47 pM. Scatchard's analysis of the data demonstrated two apparent classes of binding sites with apparent dissociation constants of 2 and 82 pM displaying 280 and 3400 binding sites, respectively. The binding was specific; half-displacement was observed with a 2-fold excess of unlabeled VAS. The structurally related **platelet**-derived growth factor did not compete in a radioreceptor assay. I-125-VAS was displaced by suramin and not by heparin. I-125-VAS was covalently cross-linked to its cell surface receptor on intact bovine adrenal cortex-derived capillary endothelial cells using the homobifunctional agents ethylene glycol bis(**succinimidyl** succinate) or **disuccinimidyl** tartarate. A major macromolecular species with an apparent molecular mass of 230,000 Da was labeled under reducing and nonreducing conditions. These data demonstrate the existence of a specific binding protein for VAS and an estimation of the size at 185,000 Da.

L78 ANSWER 36 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-712451 [67] WPIX
DOC. NO. CPI: C2003-195826
TITLE: Biodegradable biocompatible polyketal, useful in biomedical preparation e.g. fiber, comprises repeat structural units containing ketal group having one ketal oxygen atom within polymer main chain, and hydrophilic or pharmaceutical group.
DERWENT CLASS: A25 A96 B05 B07 D21
INVENTOR(S): PAPISOV, M I
PATENT ASSIGNEE(S): (GEHO) GEN HOSPITAL CORP
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003059988	A2	20030724	(200367)*	EN	59

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003059988 A2		WO 2003-US1017	20030114

PRIORITY APPLN. INFO: US 2002-348333P 20020114

AB WO2003059988 A UPAB: 20031017

NOVELTY - A biodegradable biocompatible polyketal (I) comprises repeat structural units containing:

(i) at least one ketal group, where at least one ketal oxygen atom is within the polymer main chain; and

(ii) at least one hydrophilic group or pharmaceutically useful group.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a crosslinked biodegradable biocompatible polyketal (II) comprising (I);

(2) preparation of (I) involving: (a) reacting an oxidizing agent with a polysaccharide to form a biodegradable biocompatible polyketal aldehyde, and (b) optionally treating the aldehyde with a reagent (R1) to form (I) and (c) optionally repeating step (b) until the desired functionalization of (I) is achieved;

(3) preparation of (II) involving steps (a) - (c) followed by reaction of (I) with a crosslinking agent (CA1); or step (a) followed by reacting the aldehyde intermediate with a cross linking agent (CA2); or (a1) reacting an initiator with a compound of formula (III) to form a polymer intermediate of formula -(O-C1(P1)(P2)-O-C2(P3)(P4)-Px(P5)(P6)-)n (preferably carboxylic ester, alkoxy group, thioester, thioether, vinyl group or a haloalkyl), optionally (a2) reacting the polymer intermediate with (R1) to form a second polymer intermediate and (a3) repeating step (a2) until the desired functionalization of the polymer intermediate is achieved, and (a4) reacting the biodegradable biocompatible polyketal formed in step (a3) with a crosslinking agent (CA3);

(4) a composition (A1) comprising either the macromolecular product (preferably the macromolecular product of (I) or (II)), of the lateral cleavage of a polysaccharide, where at least one carbon-carbon bond is cleaved in all the carbohydrate moieties of the polysaccharide;

(5) a composition (A2) comprising (I) associated with a therapeutic agent. The therapeutic agent is incorporated into and released from the matrix of (I) by degradation of the matrix or diffusion of the therapeutic agent out of the matrix over a period of time;

(6) a composition comprising an interface component and a macromolecule, micelle, liposome or a surface attached to the interface component;

(7) a method of administering a therapeutic agent, which is associated with and released from (I) by degradation of the polymer matrix or diffusion of the agent out of the matrix over a period of time;

(8) a chiral polymer comprising repeat units containing at least one ketal group, where at least one ketal oxygen atom is within the polymer main chain and at least one chiral group;

(9) a crosslinked chiral polyketal comprising the chiral polymer;

(10) a composition (A3) comprising the chiral polymer **covalently** bonded to an inorganic support material (s1) either directly or via a spacer grouping;

(11) preparation of the chiral polymer involving reacting an oxidizing agent with polysaccharide to form a polyketal aldehyde, and optionally (ia) treating the aldehyde with (R1) to form a polyketal, (ib)

repeating the treating step until the desired functionalization of the polyketal is achieved and (ic) reacting the polyketal with a chiral reagent to form the chiral polymer;

(12) separation of optical isomers involving using the chiral polymer, optionally bonded to (s1); and

(13) a chiral compound, which is a depolymerization product of the chiral polyketal or polymer.

P1, P2 = optionally protected organic moiety and includes a carbon atom **covalently** attached to carbon one (C1);

Px = organic moiety which includes a carbon atom **covalently** attached to carbon two (C2);

n = integer;

P3 - P6 = H, optionally protected organic moiety, protected hydrophilic group or pharmaceutically useful group.

At least one of P1 - P6 is a protected hydrophilic group or pharmaceutically useful group.

ACTIVITY - Vulnerary; Dermatological; Ophthalmological; Cardiant; Gastrointestinal-Gen.

MECHANISM OF ACTION - None given in the source material.

USE - In cross-linked biodegradable biocompatible polyketals; in interface components; in biomedical preparation e.g. fiber, gel or solution (claimed); for treating animals; in chromatographic applications e.g. in chiral separations; in pharmaceutical formulations as excipients, medical devices, implants and packaging/delivery of therapeutic, diagnostic and prophylatic agents; in biomedical applications e.g. pharmacology, bioengineering, wound healing and dermatology/cosmetics; and medical applications e.g. table coatings, **plasma** substitutes, gels, contact lenses, surgical implants, systems for controlled drug release, as ingredients of eyedrops, wound closure applications (sutures, staples), orthopedic fixation devices (e.g. pins, rods, screws, tacks, ligaments), dental applications (e.g. guided tissue regeneration), cardiovascular applications (e.g. stents, grafts), intestinal applications (e.g. anastomosis rings), implantable drug delivery devices and matrices, bioresorbable templates for tissue engineering and long circulating and targeted drugs; and for in vivo monitoring with a diagnostic label.

ADVANTAGE - The polyketals exhibit adequate biodegradability and biocompatibility, hydrophilicity, bioadhesivity in vivo and minimal toxicity, for biomedical use. The polymeric materials effectively and inexpensively allow access to useful chiral compounds. The reactants used to form the polyketals are readily available or can be synthesized using prior art methods. Polysaccharides used for lateral cleavage with conversion to acyclic polyketals are available from plants or are manufactured from prior art methods. Also the resultant polyketals can be modified to obtain products with desirable properties. The biocompatibility of the polyketals is of higher degree as compared to the polysaccharides from which they are derived since they generally do not contain cyclic carbohydrates, which are potentially receptor recognizable or immunogenic. The polyketals are valuable alternative source for chiral compounds.

Dwg.0/4

L78 ANSWER 37 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-636518 [60] WPIX
DOC. NO. CPI: C2003-173910
TITLE: New pseudo antibody used for preventing ischemia and inhibiting stenosis comprises organic group **covalently** coupled to target group.
DERWENT CLASS: A96 B02

INVENTOR(S): HEAVNER, G A; HEAVNER, G
PATENT ASSIGNEE(S): (HEAV-I) HEAVNER G A; (CENZ) CENTOCOR INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003049684	A2	20030619	(200360)*	EN	33

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

US 2003211078 A1 20031113 (200382)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003049684	A2	WO 2002-US38839	20021204
US 2003211078	A1 Provisional	US 2001-336707P	20011207
		US 2002-309722	20021204

PRIORITY APPLN. INFO: US 2001-336707P 20011207; US 2002-309722 20021204

AB WO2003049684 A UPAB: 20030919
NOVELTY - Pseudo antibody comprises an organic group **covalently** coupled to at least three identical target binding groups or at least 2 different target binding groups. The target binding groups comprise a protein, peptide, peptidomimetic or non-peptide molecule that binds to a specific targeted biological molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical composition (C1) which comprises a multivalent pseudo antibody comprising at least 2 target binding groups **covalently** coupled to a functional molecule;

(2) a pharmaceutical composition which comprises a dimerized peptidomimetic that exhibits enhanced binding to an erythropoetin receptor as compared to its monomered peptidomimetic; and

(3) a molecule that binds to a primary biological molecule, having at least one characteristic comprising a multivalent structure with enhanced avidity, increased molecular size with extended circulating half-life, specific binding to multiple compounds by a single molecule, and/or incorporation of carriers such as lipids, fatty acids, carbohydrates and steroids, that can bind to molecules other than the primary biological molecules and affect distribution to specific locations.

ACTIVITY - **Antiangiogenetic**; Vasotropic; Cytostatic.

MECHANISM OF ACTION - None given.

USE - Used for inhibiting stenosis and/or restenosis following a vascular intervention procedure, for preventing ischemia, for inhibiting growth and/or metastasis of tumors, for inhibiting **angiogenesis** and a process mediated by the binding of ligand to GPIIb/IIIa and/or alpha v beta 3 expressed on **plasma** membrane of cell (claimed).

ADVANTAGE - The pseudo antibody exhibits increased avidity compared to the unmodified target binding group from which it is derived. The pseudo antibody has improved circulatory half-life, increased avidity, increased affinity and multifunctionality.

Dwg.0/0

L78 ANSWER 38 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-449156 [42] WPIX
DOC. NO. NON-CPI: N2003-358406
DOC. NO. CPI: C2003-119182
TITLE: Composition useful for the treatment of bone injuries and as a delivery device to administer bioactive agents comprises a demineralized bone matrix and a stabilizing agent.
DERWENT CLASS: A96 B04 D16 D22 E19 P34
INVENTOR(S): DIEGMAN, M; FORSYTH, N; KNAACK, D; TRAIANEDES, K; WINTERBOTTOM, J
PATENT ASSIGNEE(S): (DIEG-I) DIEGMAN M; (FORS-I) FORSYTH N; (KNAA-I) KNAACK D; (TRAI-I) TRAIANEDES K; (WINT-I) WINTERBOTTOM J; (OSTE-N) OSTEOTECH INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003030956	A2	20030417	(200342)*	EN	44
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003143258	A1	20030731	(200354)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2003030956	A2		WO 2002-US32941	20021015
US 2003143258	A1	Provisional	US 2001-329156P	20011012
		Provisional	US 2002-392462P	20020627
			US 2002-271140	20021015

PRIORITY APPLN. INFO: US 2002-392462P 20020627; US 2001-329156P 20011012; US 2002-271140 20021015

AB WO2003030956 A UPAB: 20030703
NOVELTY - A composition (I) comprises a demineralized bone matrix (DBM) and a stabilizing agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a composition (II) comprising DBM and an excipient (E1). (II) has a at least 10 (preferably at least 20, especially at least 35)% osteoinductivity than DBM alone without excipient;

(2) a composition (III) comprising DBM and (E1) having at least 25 % of the osteoinductivity of 10 micro g BMP-collagen sponge preparation;

(3) preparation of a DBM composition involving providing DBM, providing a stabilizing agent and contacting the DBM with the stabilizing agent to form a more stable DBM composition in vivo;

(4) a drug delivery device comprising DBM, a bioactive agent (B1) to be delivered adsorbed onto the matrix and a stabilizing agent;

(5) an osteoinductive composition for implantation at a bone defect

site comprises osteoinductive DBM in a carrier of hydrated polysaccharide (D1). (D1) upon hydration imparts flowability to the composition and provides an osteoinductive activity of at least 1 as measured by athymic rat model assay;

(6) a graft material comprising either bone derived particles and a starch or its combination; or calcium phosphate particles, starch or a combination of starches and a biologically active factor;

(7) an implantable bone growth inducing composition (IV) comprising a matrix, at least one growth factor and a stabilizing agent; and

(8) an implantable bone growth inducing composition (V) comprising a particulate ceramic (preferably calcium phosphate), a growth factor associated with the ceramic, and a resorbable or biodegradable polymer (preferably polysaccharide, lipid, resorbable polymer, resorbable plastic and/or their derivatives or starch). The particulated ceramic is distributed within the polymer and the osteoinductivity of the composition, which is greater than the osteoinductivity of a composition of the particulated ceramic and associated growth factor alone.

ACTIVITY - Osteopathic; Antirheumatic; Antiarthritic.

An experimental assay was carried out using six months old male New Zealand white rabbits. A non-uniting defect (2 cm) was surgically created in the bilateral ulnae of all rabbits. After complete periostectomy, thorough defect wash and partial diaphyseal wash, grafting was implanted via open surgical technique into each defect of the test group (administered with demineralized bone matrix and starch) and the control group of rabbits (administered with starch alone). When anesthesia was achieved, both forelimbs were shaved and prepared with the rabbit supine position. Longitudinal incisions were made over both ulnae and the diaphysis portion of the ulna was exposed. The distal osteotomy was made 1 cm from the ulnocarpal joint and the proximal osteotomy made 3 cm from the ulnocarpal joint to create 2 cm defect. The osteotomies were created and the resultant loose block of diaphyseal bone was excised with its periosteum intact. After irrigation with sterile saline to remove **blood**, bone and marrow remnants, the test/control implant material was placed in the defect. The deep fascial layer was closed, followed by skin closure. A post-operative dressing/splint was applied and removed on the fourth post-operative day. Antero-posterior radiographs were obtained immediately post-operatively and additional radiographs were taken at 3, 6, 9, and 12 weeks. High resolution radiographs were taken of both limbs after excision and cleaned of soft tissue at either 6 or 12 weeks. In vivo radiographs at 3 weeks indicated bone formation was evident in the test formulation. At 6 weeks, trabeculation was observed and almost complete bridging of the critical-sized defect with the test formulation. Hence it was concluded that the test formulation improved the rate at which bone formation developed.

MECHANISM OF ACTION - Bone growth promoter.

Test details described but no relevant biological data given.

USE - For the treatment of bone defects caused by injuries, diseases (e.g. rheumatoid arthritis), wounds, surgery (e.g. joint replacement surgery). As a delivery device to administer bioactive agents (e.g. antibiotic, antineoplastic agents, growth factors, hematopoietic factors, nutrients, osteoinductive growth factors); for repairing bone fractures (e.g. fractures in ethmoid, frontal, nasal, occipital, parietal bones etc), and in the fusion of vertebrae. Also useful in orthopaedic, neurosurgical, cosmetic and oral and maxillofacial surgical procedures (e.g. repair of simple and compound fractures, and non-unions, external and internal fixations, joint reconstruction such as arthrodesis, general arthroplasty, cup arthroplasty of the hip, femoral and humeral head replacement, femoral head surface replacement and total joint replacement,

repairs of the vertebral column including spinal fusion and internal fixation, tumor surgery (e.g. deficit filling), discectomy, laminectomy, excision of spinal cord tumors, anterior cervical and thoracic operations, repair of spinal injuries, scoliosis, lordosis and kyphosis treatments, intermaxillary fixation of fractures, mentoplasty, temporomandibular joint replacement, alveolar ridge augmentation and reconstruction, inlay bone grafts, implant placement and revision and sinus lifts.

ADVANTAGE - The stabilizing agents extend the half-life of the DBM activity in vivo and enhance the osteoinductivity of the compositions resulting in improved bone formation ability as compared to prior art compositions. The excipient slows the release rate or extends the osteoinductivity lifetime of the DBM. The osteoinductive agents are protected from degradation and diffusion out of the composition. The osteoinductive factors are activated in a controlled time release manner. The compositions have improved shape-retaining characteristics, which contribute to the overall efficacy of the DBM compositions.
Dwg.0/6

L78 ANSWER 39 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-008897 [01] WPIX
DOC. NO. CPI: C2004-002242
TITLE: New molecular carrier useful for introducing substance e.g. pharmacological agent or genetic material into cells, comprising central multivalent core to which several adduct molecules are bonded.
DERWENT CLASS: A96 B04 B05 B07 D16
INVENTOR(S): CHU, Y L; LAI, W; LI, F Q; QIU, J; ZHU, S
PATENT ASSIGNEE(S): (CHUY-I) CHU Y L; (LAIW-I) LAI W; (LIFQ-I) LI F Q; (QIUJ-I) QIU J; (ZHUS-I) ZHU S
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003068379	A1	20030410	(200401)*		30

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003068379	A1 Provisional	US 2001-310492P	20010808
		US 2002-137355	20020503

PRIORITY APPLN. INFO: US 2001-310492P 20010808; US 2002-137355 20020503

AB US2003068379 A UPAB: 20040102
NOVELTY - A molecular carrier (I) comprising a central multivalent core to which several adduct molecules are bonded, is new.

DETAILED DESCRIPTION - A molecular carrier (I) of formula (F1), (F2) and (F3), comprising a central multivalent core to which several adduct molecules are bonded, is new.

Adduct = residue of an amino acid;
n = integer of 2 or greater;
m = 0 or a positive integer; and
p = positive integer.

INDEPENDENT CLAIMS are also included for the following:
(1) a pharmacological agent/molecular carrier complex (II) comprising

(I) and a pharmacological agent that is associated with at least one of the adduct moieties;

(2) a genetic material/molecular carrier complex (III) comprising (I) and genetic material which is associated with one of the adduct moieties;

(3) forming (M1) a molecular carrier by **covalently** bonding several adduct molecules to a central multivalent core molecule by reacting a nucleophilic group on each adduct molecule with an electrophilic group on the multivalent core molecule, where the multivalent core molecule comprises electrophilic groups;

(4) forming (M2) a molecular carrier comprising **covalently** bonding several adduct molecules to a central multivalent core molecule by reacting an electrophilic group on each adduct molecule with a nucleophilic group on the multivalent core molecule, where the multivalent core molecule comprises nucleophilic groups, and is chosen from benzene-tetramine, a tri(carboxymethyl)amine, ((Lys)2Lys)3-(TFA), where TFA is a tri-functional amine, diethylaminetriamine, triethylenetetramine, Tris(hydroxymethyl)aminomethane (TRIS), and NH2((CH2)nNH)m(CH2)n NH2, where n and m are integers which may vary throughout the molecule;

(5) a molecular carrier made by (M1) or (M2), and (II) and (III) produced by (M1); and

(6) (II) and (III) comprising a molecular carrier made by (M2).

USE - (I) is useful for introducing a substance into cells by incubating cell(s) with (I) associated with a pharmacological agent (e.g. non-peptide drugs, proteins, peptides, steroids or hormones) or a genetic material, for in vivo transfection of cells, comprising administering (I) associated with a pharmacological agent or a genetic material, into the cells. (I) is also useful for performing gene therapy by administering a gene therapy agent comprising (I) associated with a genetic material such as an expression vector containing a DNA segment encoding a protein or an anti-sense oligonucleotide to a human or animal. The gene therapy agent (I) is useful for improving the pharmacokinetic profile of a pharmacological agent. (I) may be used to conjugate pharmacological agent(s).

ADVANTAGE - (I) provides a drug delivery vehicle that can improve the pharmacokinetics or pharmacological agent.

Dwg.0/15

L78 ANSWER 40 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-656903 [75] WPIX
CROSS REFERENCE: 2002-010703 [01]
DOC. NO. CPI: C2001-193259
TITLE: New glycyl lysine derivatives chemically attached to a linking group, useful as integrin alphaVbeta3 antagonists for inhibiting **angiogenesis** and tumor growth.
DERWENT CLASS: B05
INVENTOR(S): BOGER, D L; CHERESH, D A
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST; (SCRI) SCRIPPS RES INC; (BOGE-I) BOGER D L; (CHER-I) CHERESH D A
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001072699	A1	20011004	(200175)*	EN	59

RW: AT BE CH CY DE EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001051018 A 20011008 (200208)
NO 2002004576 A 20021120 (200307)
NO 2002004578 A 20021120 (200307)
EP 1276713 A1 20030122 (200308) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
KR 2002084258 A 20021104 (200320)
CZ 2002003510 A3 20030312 (200324)
KR 2002091156 A 20021205 (200324)
SK 2002001484 A3 20030401 (200331)
US 2003083519 A1 20030501 (200331)
JP 2003528850 W 20030930 (200365) 65
HU 2003001797 A2 20030929 (200369)
CN 1441777 A 20030910 (200380)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001072699	A1	WO 2001-US9756	20010327
AU 2001051018	A	AU 2001-51018	20010327
NO 2002004576	A	WO 2001-US9785	20010327
		NO 2002-4576	20020924
NO 2002004578	A	WO 2001-US9756	20010327
		NO 2002-4578	20020924
EP 1276713	A1	EP 2001-924359	20010327
		WO 2001-US9756	20010327
KR 2002084258	A	KR 2002-712724	20020926
CZ 2002003510	A3	WO 2001-US9756	20010327
		CZ 2002-3510	20010327
KR 2002091156	A	KR 2002-712720	20020926
SK 2002001484	A3	WO 2001-US9756	20010327
		SK 2002-1484	20010327
US 2003083519	A1	WO 2001-US9756	20010327
		US 2002-240141	20020927
JP 2003528850	W	JP 2001-570612	20010327
		WO 2001-US9756	20010327
HU 2003001797	A2	WO 2001-US9756	20010327
		HU 2003-1797	20010327
CN 1441777	A	CN 2001-809744	20010327

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001051018	A	Based on	WO 2001072699
EP 1276713	A1	Based on	WO 2001072699
CZ 2002003510	A3	Based on	WO 2001072699
SK 2002001484	A3	Based on	WO 2001072699
JP 2003528850	W	Based on	WO 2001072699
HU 2003001797	A2	Based on	WO 2001072699

PRIORITY APPLN. INFO: US 2000-192260P 20000327; US 2002-240141
20020927

AB WO 200172699 A UPAB: 20031211
NOVELTY - New glycyl lysine derivatives chemically attached to a linking

group, which bind to integrin alpha V beta 3 and block the interaction of integrin alpha V beta 3 with matrix metalloproteinase 2 (MMP2) are disclosed.

DETAILED DESCRIPTION - Glycyl lysine derivatives chemically attached to a linking group of formula (I) are new.

G1,G2 = -NH-C(O)-O-R1, -NH-C(O)-O-(CH2)v-(C6H4)-X1, -NH-C(O)-NH-(CH2)v-(C6H4)-X1, -O-C(O)-NH-(CH2)v-(C6H4)-X1, -O-C(O)-O-(CH2)v-(C6H4)-X1, or -NH-C(O)-CH2-(C6H4)-X1;

Y1, Y2 = OH, 1-4C (hydroxy)alkyl, 1-4C alkoxy, phenyl, benzyl, or NH2;

R1 = 1-4C alkyl;

t = 0-1;

X1 = halo, nitro, 1-4C alkyl, 1-4C alkoxy, or 1-4C perfluoroalkyl;

Z' = -CC-, -C6H4-, cis-CH=CH-, trans-CH=CH-, cis-CH2-CH=CH-CH2-, trans-CH2-CH=CH-CH2-, 1,4-naphthyl, cis-1,3-cyclohexyl, trans-1,3-cyclohexyl, cis-1,4-cyclohexyl, or trans-1,4-cyclohexyl;

A = H or a **covalent** bond;

m, n = 0 or 1; and

v = 1 or 2.

With the provisos that when A is H, t is 0; when A is a **covalent** bond, t is 1; when m is 0, Y1 is 1-4C hydroxyalkyl; and when n is 0, Y2 is 1-4C hydroxyalkyl.

ACTIVITY - **Antiangiogenic**; Cytostatic; Cytotoxic; Antiinflammatory.

Primary tumors were grown on CAMs (chick chorioallontoic membranes) of 9-day embryos by implantation of 5x106 CS-1 cells and incubation for 7 days. 50 mg sections of these tumors were subcultured onto fresh 9-day CAMs and allowed to implant for 24 hours before a single intravenous (i.v.) injection with 100 micro l of 100 micro M of test compounds in Hank's balanced saline solution (HBSS). Buffer alone was used as control. Tumors were incubated for 10 days, harvested and trimmed free of excess stromal tissue before determining wet weight and processing for histology. Growth of transplanted alpha V beta 3-negative CS-1 melanoma tumors on the chick CAM was significantly retarded by a single i.v. injection of compound (Ia) as was tumor weight. A gross reduction in the surface vasculature as well as the overall **blood** vessel density was evident in the tumors that had been treated with N,N'-bis-((5-(S)-carboxy-5(((4-trifluoromethyl)benzylcarbonyl)amino)-pentyl)carboxamidomethyl)benzene-1,3-dicarboxamide (Ia). This reduction in tumor vasculature was associated with significant cell death within the tumor mass, even as the control tumors showed a 6-fold increase in mass during the 10-day time frame of the assay.

MECHANISM OF ACTION - Integrin alpha V beta 3 antagonist.

To identify a specific inhibitor of the binding interaction between MMP2 and integrin alpha V beta 3, solid phase receptor binding assays were performed with immobilized integrins and biotinylated MMP2. The binding of purified MMP2 was found to be entirely RGD-independent in this system, as evidenced by the lack of effect of cRGDfV on MMP2 binding to integrin alpha V beta 3, even though this peptide inhibited the interaction of alpha V beta 3, with its extracellular matrix ligand, vitronectin (VN). The binding of MMP2, but not that of VN, was completely abrogated by the compound N,N'-bis-((5-(S)-carboxy-5(((4-trifluoromethyl)benzylcarbonyl)amino)-pentyl)carboxamidomethyl)benzene-1,3-dicarboxamide (Ia), showing the specificity of (Ia) for the interaction between MMP2 and alpha V beta 3. The binding between MMP2 and tissue inhibitor of metalloproteinase 2 (TIMP2) was further not inhibited by (Ia), supporting the contention that the effect of (Ia) is restricted to the binding between MMP2 and integrin alpha V beta 3, and showing a distinction between the binding sites for

the MMP2 PEX (undefined) domain on TIMP2 and integrin alpha V beta 3.
USE - (I) can be used for inhibiting **angiogenesis** in tumor tissue and inhibiting tumor growth (claimed). They can induce apoptosis in tumor cells and inhibit the interaction of MMP2 with integrin alpha V beta 3 in a host cell (claimed). They can also be used to treat other disorders involving undesired **angiogenesis**. Because the compounds bind to alpha V beta 3, they can also be used to suppress inflammatory events. Dwg.0/5

L78 ANSWER 41 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-090970 [10] WPIX
CROSS REFERENCE: 2001-007496 [01]; 2001-025008 [03]; 2001-112059 [12]
DOC. NO. NON-CPI: N2001-068963
DOC. NO. CPI: C2001-026651
TITLE: New modified anti-**angiogenic** kringle 5 peptides capable of forming conjugates with **blood** proteins, useful for treating **angiogenesis**, inappropriate invasion of vessels or cancers in humans or mammals.
DERWENT CLASS: B04 C03 U11
INVENTOR(S): BELIVEAU, R; BRIDON, D P; HUANG, X; RASAMOELISOLO, M; THIBAUDEAU, K
PATENT ASSIGNEE(S): (CONJ-N) CONJUCHEM INC
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000070665	A2	20001123	(200110)*	EN	82
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000047748	A	20001205	(200113)		
EP 1171582	A2	20020116	(200207)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003500341	W	20030107	(200314)		91
AU 764103	B	20030807	(200362)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000070665	A2	WO 2000-IB763	20000517
AU 2000047748	A	AU 2000-47748	20000517
EP 1171582	A2	EP 2000-929748	20000517
		WO 2000-IB763	20000517
JP 2003500341	W	JP 2000-619018	20000517
		WO 2000-IB763	20000517
AU 764103	B	AU 2000-47748	20000517

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000047748	A	Based on	WO 2000070665
EP 1171582	A2	Based on	WO 2000070665
JP 2003500341	W	Based on	WO 2000070665
AU 764103	B	Previous Publ.	AU 2000047748
		Based on	WO 2000070665

PRIORITY APPLN. INFO: US 1999-134406P 19990517

AB WO 200070665 A UPAB: 20030928

NOVELTY - A modified anti-**angiogenic** peptide comprising a reactive group that reacts with amino groups, hydroxyl groups or thiol groups on **blood** components to form stable **covalent** bonds, is new. The reactive group is selected from **succinimidyl** or **maleimido** groups.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising a derivative kringle 5 peptide or its analog, where the derivative comprises the reactive, or a composition having a derivative of an anti-**angiogenic** peptide, where the derivative has a **maleimido** group that reacts with a thiol group on human **serum albumin** (HSA) to form a **covalent** bond;

(2) a derivative of a kringle 5 peptide, where the derivative comprises a **maleimido** group that reacts with a thiol group on human **serum albumin** (HSA) to form a **covalent** bond; and

(3) a modified kringle 5 peptide selected from one of the sequences (I-XL).

ProArgLysLeuTyrAspLys (I); TyrThrThrAsnProArgLysLeuTyrAspTyrLys (II); ArgAsnProAspGlyAspValGlyGlyProTrpAlaTyrThrThrAsnProArgLysLeu-TyrAspTyrLys (III); ArgAsnProAspGlyAspValGlyGlyProTrpLys (IV); ProArgLysLeuTyrAspTyrLys (V); TyrThrThrAsnProArgLysLeuTyrAspTyrLys (VI); TyrThrThrAsnProArgLysLeuTyrAspTyr (VII); ArgAsnProAspGlyAspValGlyGlyProTrpAlaTyrThrThrAsnProArgLysLeu-TyrAspTyr (VIII); ArgLysLeuTyrAspTyrLys (IX); ArgLysLeuTyrAspTyr (X); ProArgLysLeuTyrAspLys (XI); ProArgLysLeuTyrAsp (XII); ProArgLysLeuTyrAspTyrLys (XIII); ProArgLysLeuTyrAspTyr (XIV); or ArgAsnProAspGlyAspValGlyGlyAspValGlyGlyProTrp (XV). NAc-(I)-NH2 (XVI); NAc-(IX)-NH2 (XVII); NAc-(II)-NH2 (XVIII); NAc-(III)-NH2 (XIX); NAc-(IV)-NH2 (XX); NAc-(V)-NH2 (XXI); 3-**maleimidopropionic** acid-aminoethoxyethoxyacetic acid (MPA-AEEA)-(XIV)-NH2 (XXII); (MPA)-(XIV)-NH2 (XXIII); NAc-(VI)-(N epsilon -MPA)-NH2 (XXIV); (MPA-AEEA)-(VII)-NH2 (XXV); (MPA)-(VII)-NH2 (XXVI); NAc-(III)-(N epsilon -MPA)-NH2 (XXVII); (MPA-AEEA)-(VIII)-NH2 (XXVIII); (MPA)-(VIII)-NH2 (XXIX); NAc-(IV)-(N epsilon -MPA)-NH2 (XXX); (MPA-AEEA)-ArgAsnProAspGlyAspValGlyGlyProTrp-NH2 (XXXI); (MPA)-ArgAsnProAspGlyAspValGlyGlyProTrp-NH2 (XXXII); NAc-(IX)-(N epsilon -MPA)-NH2 (XXXIII); (MPA-AEEA)-(X)-NH2 (XXXIV); (MPA)-(X)-NH2 (XXXV); NAc-(XI)-(N epsilon -MPA)-NH2 (XXXVI); (MPA-AEEA)-(XII)-NH2 (XXXVII); (MPA)-(XII)-NH2 (XXXVIII); NAc-(XIII)-(N epsilon -AEEA-MPA)-NH2 (XXXIX); or NAc-(XIII)-(N epsilon -AEEAn-MPA)-NH2 (XL).

ACTIVITY - Anti-inflammatory; vasotropic; cytostatic; antirheumatic; antipsoriatic; antidiabetic; antiarteriosclerotic; osteopathic.

No biological data is given.

MECHANISM OF ACTION - **Angiogenesis** inhibitor.

USE - The compositions are useful for treating **angiogenesis** in a human, where the derivative is reacted with **blood** proteins. The compositions is also useful for manufacturing a medicament extending the in vivo half-life of a kringle 5 peptide in a patient to provide an

anti-**angiogenic** effect. (All claimed). In particular, the modified kringle 5 peptide is useful for treating inflammatory disorders (e.g. immune and non-immune inflammation, chronic articular rheumatism or psoriasis), disorders associated with inappropriate or inopportune invasion of vessels (e.g. diabetic retinopathy, **neovascular** glaucoma, restenosis, capillary proliferation in atherosclerotic plaques or osteoporosis), or cancer associated disorders (e.g. solid tumors, solid tumor metastases, angiofibromas, retrolental fibroplasia, hemangiomas, Kasposi's sarcoma or other cancers requiring **neovascularization** to support tumor growth). The peptide is useful for treating these diseases in mammalian or human patients.
Dwg.0/0

L78 ANSWER 42 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-182339 [16] WPIX
DOC. NO. CPI: C2000-056996
TITLE: **Immunogenic** forms of immunosuppressive or **angiogenic** proteins, used for treatment or prevention of cancer, are modified versions of viral proteins.
DERWENT CLASS: B04 D16
INVENTOR(S): ZAGURY, J; ZAGURY, J F; ZAGURY, D A
PATENT ASSIGNEE(S): (VACS-N) VACS INT; (VACS-N) VACS INT SARL; (NEOV-N) NEOVACS
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000003732	A1	20000127	(200016)*	FR	57
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
FR 2781158	A1	20000121	(200018)		
AU 9941496	A	20000207	(200029)		
EP 1096953	A1	20010509	(200128)	FR	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
US 2004001852	A1	20040101	(200402)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000003732	A1		WO 1999-FR1423	19990615
FR 2781158	A1		FR 1998-9046	19980715
AU 9941496	A		AU 1999-41496	19990615
EP 1096953	A1		EP 1999-925094	19990615
			WO 1999-FR1423	19990615
US 2004001852	A1	Div ex	WO 1999-FR1423	19990615
		Div ex	US 2001-743700	20010116
			US 2003-465645	20030620

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9941496	A	Based on	WO 2000003732
EP 1096953	A1	Based on	WO 2000003732

PRIORITY APPLN. INFO: FR 1998-9046 19980715

AB WO 200003732 A UPAB: 20000330

NOVELTY - Use of a protein (A), or its fragment, is derived from a protein (A') produced by cancer, virally infected or immune system cells, to produce an anticancer composition with localized anti-immunosuppressive or anti-**angiogenic** activity.

DETAILED DESCRIPTION - (A') is an immunosuppressive or **angiogenic** agent with localized action and is modified, to render it inactive by at least 70%, by chemical and/or physical treatments, genetic recombination or by adjuvant conditioning, the (A) produced retains recognition by anti-(A') antibodies and is sufficiently immunogenic to generate antibodies that neutralize or block (A').

INDEPENDENT CLAIMS are also included for the following:

(1) immunogenic compound (I) that is (A) other than carboxymethylated Tat protein of human immunodeficiency virus (HIV)-1, or its fragments;

(2) preparation of (I);

(3) antibody (Ab) directed against proteins with local immunosuppressant or **angiogenic** activity (except HIV-1 Tat) and expressed by cancer cells, produced by immunizing a mammal with (I);

(4) F(ab')2 and F(ab) fragments of Ab;

(5) pharmaceutical composition containing Ab or its fragments, and

(6) vaccines containing (I).

ACTIVITY - Anticancer; anti-**angiogenic**; anti-immunosuppressive.

MECHANISM OF ACTION - (A) generate antibodies that block or neutralize (A'), eliminating the immunosuppressive or **angiogenic** activities of these proteins. When peripheral **blood** mononuclear cells were incubated with 10 mu g/ml of native Tat protein, proliferation was reduced to only 20% of that in a control. In presence of the same concentration of a Tat that had been reacted with iodoacetic acid, proliferation was 95% of control levels, indicating that derivatization had eliminated the immunosuppressant action of Tat. The derivatized peptide induced antibodies when injected into mice at about the level as the native protein.

USE - (A) are used as anticancer agents (active immunization) or to raise antibodies for similar use (passive immunization). Especially they are used to treat virus-induced cancers, e.g. acute T-cell leukemia, cancer of the cervix uteri, Burkitt lymphoma and Kaposi sarcoma.

Dwg.0/5

L78 ANSWER 43 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-312872 [26] WPIX
DOC. NO. CPI: C1999-092336
TITLE: Bioactive materials for modulating heparin-binding growth factor activity and targeted drug delivery.
DERWENT CLASS: B04 B07
INVENTOR(S): GALLAGHER, J T; PYE, D A
PATENT ASSIGNEE(S): (CANC-N) CANCER RES CAMPAIGN TECHNOLOGY
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9921588	A1	19990506	(199926)*	EN	96

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW
AU 9910391 A 19990517 (199939)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9921588	A1	WO 1998-GB3201	19981028
AU 9910391	A	AU 1999-10391	19981028

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9910391	A	Based on	WO 9921588

PRIORITY APPLN. INFO: GB 1997-22604 19971028

AB WO 9921588 A UPAB: 19990707

NOVELTY - Bioactive materials comprise conjugate of (a) heparin-binding protein or polypeptide growth factor and (b) heparin or heparan sulfate (HS) of oligosaccharide coupled together through **covalent** bonds.

DETAILED DESCRIPTION - INDEPENDENT CLAIM are also included for

(1) A one-step preparation of bioactive material by treating HS oligosaccharide preparation with crosslinking reagents to form **succinimide** ester derivative in presence of growth factor and purifying;

(2) A pharmaceutical formulation comprising the above bioactive material; and

(3) A method for manufacturing a medical preparation comprising the above bioactive material;

ACTIVITY - Healing promotion; tissue repair promotion; cell growth control; cell proliferation control.

MECHANISM OF ACTION - HB-EGF modulation; FGF inhibitor; FGF stimulator. Binding affinity of bFGF-oligosaccharide conjugates was checked by filter-binding assay. Native growth factor or growth factor/HS oligosaccharide conjugate material (4 mu g) was applied to nitrocellulose membrane filters in binding buffer (10 mM Tris-HCl; pH 7.3). The filters were washed with 2M sodium chloride (NaCl; 10 ml) in binding buffer to remove any non-crosslinked oligosaccharide present and were then equilibrated by washing with binding buffer. Radio-labeled 3H-HS was then applied in binding buffer (5 ml) and cycled through the filter three times. The filters were then washed with binding buffer (120 ml) to remove unbound material and bound HS was released by sequential washing first with three 5-ml aliquots of 0.3M NaCl followed by three 5-ml aliquots of 2M NaCl in binding buffer. Fractions (5 ml) were collected and radio-labeled eluted material quantified by scintillation counting. The results showed the complex to have no high or low affinity binding capacity for HS indicating that the oligosaccharide conjugate is **covalently** linked into the growth factor's HS binding site, resulting in the site being completely obscured from further HS interactions.

USE - Used in therapeutic pharmaceutical formulations to modulate heparin-binding growth factor activity in mammals and deliver drug or

other therapeutic agent to mammals (claimed). Used to modulate growth factor activity and for targeted drug delivery in course of therapeutic treatment (claimed). Used to modify drugs or prodrugs to facilitate administration to mammals and targeted delivery to cells with specific growth factor receptors (claimed). Used as active FGF-activity stimulating agent to promote healing or tissue repair in mammals in connection with wound healing, bone healing, nerve regeneration, duodenal or venous ulcers, ocular and retinal disorders, atherosclerosis, ischemia or other conditions requiring tissue repair or to protect tissues against serious damaged during radiation treatment. Used as active FGF-activity inhibitor to control or reduce cell growth or proliferation in mammals in connection with diabetic retinopathy, capsular opacification, proliferative vitreoretinopathy, tumor **angiogenesis**, cancer-cell growth and metastasis, rheumatoid arthritis, degenerative muscular disorders (mild muscular dystrophy), Alzheimer's disease, viral infections (Herpes Simplex type 1), restenosis following angioplasty other conditions in which FGF activity inhibition is required.

ADVANTAGE - **Covalent** bonding between growth factor and oligosaccharide still allows growth factor to bind to its cell surface signal-transducing receptors on target cells and even when diminished, still mimics, to some extent, that of unbound or native growth factor. More resistant to proteolytic degradation and thermal inactivation. Oligosaccharide is varied to produce effects of stimulation/enhancement or inhibition of the growth factor's normal activity. The direct **covalent** linking of the growth factor to the oligosaccharide provides better bioavailability and enhanced targeting.

dp12/basic FGF (bFGF) crosslinked monomer conjugates and native bFGF (0.5 mu g) were mixed in phosphate-buffered saline (50 mu l) containing, as detergent, 3-((cholamidopropyl)-dimethylammonio)-1-propane-sulfonate (CHAPS; 1%) before addition of trypsin (4 mu l; 2 mg/ml). The reaction mixtures were incubated for 24 hours at 37 deg. C, aliquots were removed and analyzed by 12% SDS polyacrylamide electrophoresis (PAGE) and immunodetection. Results showed that dp12/bFGF crosslinked monomer conjugates were significantly more resistant to proteolytic degradation compared to the native bFGF, which was extensively degraded.

L78 ANSWER 44 OF 44 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1988-119357 [17] WPIX
CROSS REFERENCE: 1988-056503 [08]; 1989-206431 [28]; 1990-067060 [09]; 1990-375338 [50]
DOC. NO. NON-CPI: N1988-090685
DOC. NO. CPI: C1988-053541
TITLE: Bio material with desired biocompatible surface - useful for production of substitute **blood** vessels, lenses, electrodes, catheters etc..
DERWENT CLASS: A18 A25 A82 A96 B07 D22 P32 P34 P81
INVENTOR(S): GUIRE, P E
PATENT ASSIGNEE(S): (BIOM-N) BIO METRIC SYSTEMS INC; (BIOM-N) BIO-METRIC SYSTEMS INC
COUNTRY COUNT: 17
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8802623	A	19880421	(198817)*	EN	50
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DK JP NO					
AU 8782320	A	19880506	(198830)		

EP 326579	A	19890809 (198932)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE				
JP 02500250	W	19900201 (199011)		
US 4979959	A	19901225 (199103)		14
CA 1305068	C	19920714 (199234)		
US 5263992	A	19931123 (199348)		16
EP 326579	B1	19950111 (199506)	EN	30
R: AT BE CH DE FR GB IT LI LU NL SE				
EP 326579	A4	19891227 (199509)		
DE 3750989	G	19950223 (199513)		
JP 2741378	B2	19980415 (199820)		15
JP 10179726	A	19980707 (199837)		20
JP 2981488	B2	19991122 (200001)		20

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 8802623	A		WO 1987-US2675	19871016
EP 326579	A		EP 1987-907467	19871016
JP 02500250	W		JP 1987-506895	19871016
US 4979959	A		US 1989-349884	19890505
CA 1305068	C		CA 1987-549485	19871016
US 5263992	A	Cont of	US 1986-920567	19861017
		Div ex	US 1989-349884	19890505
		Cont of	US 1990-558164	19900725
			US 1991-783711	19911024
EP 326579	B1		EP 1987-907467	19871016
			WO 1987-US2675	19871016
EP 326579	A4		EP 1987-907467	
DE 3750989	G		DE 1987-3750989	19871016
			EP 1987-907467	19871016
			WO 1987-US2675	19871016
JP 2741378	B2		JP 1987-506895	19871016
			WO 1987-US2675	19871016
JP 10179726	A	Div ex	JP 1987-506895	19871016
			JP 1997-287546	19871016
JP 2981488	B2	Div ex	JP 1987-506895	19871016
			JP 1997-287546	19871016

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5263992	A	Div ex	US 4979959
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DE 3750989	G	Based on	EP 326579
		Based on	WO 8802623
JP 2741378	B2	Previous Publ.	JP 02500250
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JP 2981488	B2	Previous Publ.	JP 10179726

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AB WO 8802623 A UPAB: 20000105
Biomaterial having biocompatible surface is prepared by using a solid surface of the biomaterial, a biocompatible agent (I) and a chemical

linking moiety possessing a photochemically reactive gp. capable on activation of bonding to the solid surface, and possessing a different reactive gp. capable of binding to the molecules of the biocompatible agent. One of the gps. is unresponsive to a stimulus to which the other gp. responds.

One of the gps. of the linking moiety is activated to cause it to react, then the other reactive gp. is activated to **covalently** bind the linking moiety to the solid surface to give a sufficient population density of molecules of (I) to shield the solid surface effectively and to give a biocompatible surface.

USE/ADVANTAGE - The biomaterial may be used for the construction of substitute **blood** vessels, synthetic and intraocular lenses, electrodes, catheters and other devices for medical use.
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